



**School of Applied Medical Science**

**Department of Pharmaceutical & Chemical Engineering**

**Pharmaceutical Technology-Liquid Forms Lab**

**Course code PCE373**

# Preface

The laboratory course will serve as a foundation course for applying the knowledge and skills to practice the science of pharmaceutical compounding. Special emphasis is given on preparation of dosage formulations in a laboratory scale while keeping the industrial practice in view. Evaluation tests are also included for every formulation.

The pharmaceutical technology lab is scheduled to meet once each week for 3 hours. During the lab sessions you will be required to complete an experimental procedure and the questions associated with the material, unless otherwise instructed. It is your responsibility to ensure you have all the necessary results and to have completed any calculations before leaving the lab.

Each lab session is divided into three main parts; *Discussion*, the *Experimental results* which are to be recorded while following the experimental methodology and finally the *Post-laboratory* questions. All three sections have to be submitted to your TA or instructor before leaving the lab. This will be discussed in further details at a later stage.

During the first lab meeting, you will be introduced to some of the safety equipment in the lab as well as the rules and regulations for your class. *Close attention must be paid to this discussion so that you can react properly in case of an emergency.*

## Preparation for the laboratory

Each experiment in this lab manual has a clear *Objective* describing the purpose of the procedure and an *Introduction* that reviews and explains in detail the theory and methods of the experiment. It is important that you fully understand these sections before beginning your lab work.

The first two sections are followed by the *Procedure* which is a clear description of the steps you will follow in performing the experiment each week. It is written to be clear and concise as possible and you must read all of it each week before coming to class.

You will be required to bring a lab coat and protective eyewear (goggles or glasses with side-shields) as well as a calculator. Please note you will not be allowed to enter the lab if you do not come prepared with a lab coat and goggles.

## Laboratory Reports

For each experiment, you will be expected to complete a series of *Post-Laboratory* questions. After each lab, your instructor will ask that you complete the *Post-Laboratory* exercises to summarize your results each week. This means to analyze the data you collected, analyze the sources of error, and make conclusions about the work you did. This should consist of the following:

1. Data Tables, calculations and results
3. Laboratory questions
4. Short summary of your results

For Some Experiments the lab instructors will ask each student to hand out a complete Lab Report, which includes:

Objectives.

Introduction.

Chemicals, glassware, and equipment.

Procedure.

Results, calculations and discussion.

Conclusion.

References.

# Safety

Pharmaceutics is an experimental science. As a student of chemical and pharmaceutical engineering you will be handling a variety of chemicals, some of which can be harmful. However following the correct safety procedures minimizes the risk of harm to you and your colleagues. It is vital that you approach your lab work calmly and studiously to avoid any mishaps. If you are ever in doubt on the correct safety procedure ask your instructor or TA.

As previously mentioned, during your first lab session you will be given a brief tour of your laboratory where you will be shown the locations of various pieces of emergency equipment that are there for your safety. Detailed information on specific safety procedures can be found below.

## Protection for Your Eyes

It is a lab requirement that you wear protective eyewear while you are in the laboratory. Protective eyewear must be worn even if you are personally not working on an experiment. If a chemical should splash near your eyes, the eyewash fountain (see figure to the right) should be used to rinse the chemical away before it has a chance to run in behind your safety glasses.



## Protection from Fire

The danger of fire in a chemistry laboratory is real, since the lab usually has a large number of flammable liquid in it and open-flame gas burners are sometimes used for heating. With careful attention, though, the danger of fire can be reduced considerably, and even avoided completely.

Always check the lab before lighting a gas burner (Bunsen burner) to be sure that no one is pouring or using flammable chemicals near you. Since the vapors of most flammable liquids are heavier than air, be especially careful around sinks as they tend to concentrate there.

Despite of all the precautions you take, fires may still occur. The method you use to fight them depends on their size and on the substance that is burning. If only a small amount of flammable material has caught fire and there is no chance it can spread, depriving it of oxygen is the best and safest method to extinguish the flames. To do this, put a beaker over the fire and it will quickly go out. Leave the beaker in place for several minutes to ensure that the flammable material has cooled and it will not flare up again.

In the unlikely event that a larger chemical fire should occur, carbon dioxide fire extinguishers are available in the lab. When using a CO<sub>2</sub> fire extinguisher, direct the spray at the base of the fire. This not only deprives it of oxygen, but quickly cools the flammable material quickly. If this does not quickly work to extinguish the fire, immediately evacuate the laboratory and call the fire department. Be aware the CO<sub>2</sub> fire extinguishers should not be used on fires in which magnesium (or other reactive metals) are burning – this may only make the fire worse. Consult your instructor before using a fire extinguisher to be certain you have chosen the correct method.

One of the most frightening and potentially dangerous accidents in the chemistry laboratory is the igniting of a person's clothing. For this reason, certain types of clothing should never be worn in the lab, including

long flowing sleeves; clothing made of silk or other flammable fabrics; and long hair should be tied back. In the unlikely event that a student's hair or clothing catches fire, his or her colleagues must act quickly to extinguish the flames and prevent serious burns. The figure below shows the kind of safety shower you will find in our labs. This type of equipment provides a very large amount of water, very quickly to put out most types of fires.

### Protection from Burns

Simple burns occur in the laboratory when students forget that an apparatus is hot and touches it. Never touch a piece of equipment that has been heated until it has cooled for at least five minutes. Use tongs if you are unsure! Perhaps the most common accident in the lab is the tipping over of a flask or beaker while it is being heated or handled.

Another common mistake involves heating liquids in test tubes. If the contents of the tube are heated too quickly they can super-heat and blow out of the test tube causing significant damage. Ideally, heat a test tube in a beaker of boiling water, or if you must heat it directly over a heat source (like a Bunsen burner) hold it at a 45° angle, pointed away from yourself and anyone else in the lab. Gently move the tube through the flame, only briefly should it come in contact with the fire.



### Protection from Chemical Burns

Most acids, alkalis (bases) and oxidizing and reducing agent are corrosive to the skin. Since it is impossible to avoid using these substances completely, you must learn how to handle them properly and safely. As a general rule, a material's corrosiveness is related to its concentration – the higher the concentration, the more dangerous it may be. You should wash your hands frequently during lab, especially if any chemical substance is spilled on your skin.

After working with a substance that you know is particularly dangerous or corrosive, wash your hands, even if you did not spill any – you don't know if the student using the bottle before you spilled any on the outside of the container. Whenever you spill a corrosive substance on your skin you should tell your instructor immediately. If there is any sign of damage to your skin you should see a doctor as soon as possible. In the event of a chemical spill, one in which substantial portions of your body or clothing are affected, use the emergency shower.

### Protection from Toxic Fumes

Many chemical substances are volatile (easily become a gas) and have toxic vapors. Some toxic fumes can overpower you immediately (like ammonia), whereas some fumes are even more dangerous and can cause harm without realizing. Chemistry labs are equipped with fume hoods (figure to the right) that have exhaust fans to pull the vapors into the hood and away from you. Flammable solvents should also be stored in the hood to reduce the risk of fire.



### Protection from Cuts

Broken glassware should not be touched with your bare hands. Use a broom and dustpan to clean up any spills or shards of glass. Each lab has a designated place to put broken glass – do not throw broken glass into the general waste bins.

Report any cuts to your instructor immediately, no matter how minor they seem. If there is damage to your skin, you will likely be sent to see a doctor. What may seem like a scratch could become infected from the chemicals you were using and should be treated by a professional.

## **Summary of Safety Rules and Regulations**

### General Lab Rules

- Do not enter the laboratory before your instructor or TA arrives.
- Wear safety glasses and lab coat at all time when you are in the laboratory.
- Do not wear short skirts, shorts, or open-toed shoes in the laboratory.
- Do not wear scarves or neckties in the lab, because they may accidentally be ignited in the flame of a Bunsen burner.
- Students with long hair should tie it back before entering the lab, may accidentally catch fire.
- Never chew gum, eat, drink, or smoke in the laboratory.
- You will not be allowed entry into the lab if you are more than 15 min. late to the start of the session.
- You will be dismissed from the lab on the instance of your third absence.
- You are to adhere to University conduct rules at all times and any rude or dangerous behavior will result in your dismissal from all future lab sessions.
- Always listen to instruction announcements from the instructor or TA during lab sessions.

### Heating Safety Tips

- Never leave a lighted Bunsen burner unattended.
- Never heat solutions to dryness, this can sometimes cause an explosion.
- Never heat a "closed system" such as a stoppered flask.
- To heat liquids, add 2-3 boiling stones to help it heat evenly and boil smoother.

### Waste Disposal

- Always use the smallest amount of substance required for an experiment.
- Never return unused portions of chemicals to their original bottle.
- Dispose of all reaction products as directed by your instructor. In particular, observe the special disposal techniques necessary for flammable or toxic substances.
- Dispose of all glass products in the special container provided.

### Other Rules

- Never remove any chemical substance from the laboratory. This may cause expulsion from our class and from the university
- Keep your work area clean, and help keep the common areas of the laboratory clean. If you spill something in a common area, remember that this substance may injure someone else.
- Never fully inhale vapors of any substance. Waft a tiny amount of the vapor toward your nose if you need to smell it.
- Never add water to a concentrated reagent when diluting the reagent. Always add the reagent to water. The reverse may cause it to splash out on you.
- Never perform any experiment that is not specifically authorized by your instructor.
- All lab stools are to be stored beneath the lab benches when not in use.
- All personal belongings are to be stored underneath the lab bench or in the designated cupboard.

## Experiment 1

### Review of Pharmaceutical Calculations

#### INTRODUCTION:

One of the most important areas of study for the pharmacy specialist is pharmaceutical calculations. A person might know a great deal about pharmacology, but if he cannot perform a pharmaceutical calculation, that knowledge cannot be applied in a practical way. To prepare and dispense medications, you must be capable of performing a variety of pharmaceutical calculations. You must be constantly aware of one fact—an error made in a dosage calculation can harm a patient. The study of this lab will help give you the knowledge and skill required to perform many types of dosage calculations.

#### ***Potential for Error:***

One of the greatest potentials for error in prescription compounding is in the area of pharmacy math, or pharmacy calculations. Even though most of the processes are relatively simple, a misplaced decimal or "estimated" value for a medication can have serious consequences, including death. There is no excuse for ignorance in this area and, an individual unprepared to do the necessary calculations should not be involved in pharmaceutical compounding. It is of utmost importance that pharmacists be extremely well grounded in the practice of pharmaceutical calculations as there is "zero-tolerance" allowed in these vital operations.

#### **The Metric System**

The most commonly used system of weights and measures in pharmacy is the metric system. The three basic units of the metric system are the meter, the gram, and the liter. The names of the other units are formed by adding a prefix to one of the basic units. Each prefix has a numerical value as indicated below:

<u>PREFIX</u>	<u>VALUE</u>
micro - (mc) =	1/1,000,000
milli - (m) =	1/1,000
centi - (c) =	1/100 times the basic unit.
deci - (d) =	1/10
deka - (dk) =	10
hecto - (h) =	100 times the basic unit.
Kilo - (k) =	1000

The liter and the gram are the units of the metric system most used in the pharmacy. The meter is seldom used in the pharmacy. The liter is the basic unit of volume used to measure liquids in the pharmacy. One milliliter is equal to the volume of one cubic centimeter of water at 4°C. Abbreviation: L or l. 1/1000th of a liter is a milliliter, (1 ml = 1 cc)

Common conversions:

- (a) 1 liter= 1000 ml = 1000 cc      (b) 1 gallon=3785 ml  
 (c) 1 quart= 946 ml                      (d) 1 pint= 473 ml  
 (e) 1 fl oz= 30 ml (29.57)

The Gram. The gram is the basic unit of weight used to weigh solids in the pharmacy. One gram is equal to the weight of one milliliter of distilled water at 4°C. Abbreviation: Gm or g.

Common conversions:

- (a) 1 kg=1000 g                              (b) 1 g =1000 mg  
 (c) 1 mg=1000 mcg                        (d) 1 lb. =454 g  
 (e) 1 oz=28.4 g (28.35)

### Using Conversions in Problems

The main reason to convert units is to satisfy unit equality in a ratio and proportion problem.

For example: If a syrup contains 250 milligrams of tetracycline in each 5 milliliters of the syrup, how many grams of tetracycline are needed to make four liters of the syrup?

When put in a proportion, the problem would be set up as follows:

If 250 mg/5 ml= then X grams /4 liters

Prior to cross-multiplying , the units must be the same:

Changes: 250 mg = 0.25 (g)

4 L = 4000 (ml)

Only when corresponding units are the same, may the cross-multiplication take place:

$0.25 \text{ gm}/5 \text{ ml} = X\text{gm} /4000 \text{ ml}$

Then:  $5(X) = 0.25 (4000)$

$5 X=1000$

$X= 200 \text{ gm}$

**(You can also use conversion factor directly).**

### Solubility Expressions:

Expressions of strength:

- Ratio: is the relative magnitude of two like quantities thus 1: 10 = 1 part in 10 parts or 1g in 10g.
- Ratio strength: is the expression of a concentration by means of a ratio, e.g 1:10, that is; 1 part of solute in 10 parts of solution ( 1 part solute + 9 parts solvent).
- Percentage strength: is a ratio of parts per hundred, e.g. 10%
- Percentage weight in weight (w/w)
- Percentage weight in volume (w/v)
- Percentage volume in volume (v/v)

Other expressions of concentration:

- Moles & molarity
- Molality.
- Normality

## Percentage Concentrations

Expression	Symbol	Definition
Molarity	M, c	Moles (gram molecular weights) of solute in 1 liter (1000 ml) of solution.
Molality	m	Moles of solute in 1000 gm of solvent.
Normality	N	Gram equivalent weights of solute in 1 liter of solution
Mole Fraction	x	Ration of moles of solute to total moles of solute+ solvent
Percentage by Weight	% w/w	gm of solute in 100 gm of solution
Percentage by Volume	%v/v	ml of solute in 100 ml of solution
Percentage Weight in Volume	% w/v	gm of solute in 100 ml of solution

Solubility expressions

The use of percentages is a common way of expressing the concentration of a solution. It is a straightforward approach that you have used earlier when dealing with the composition of compounds. There are, however, some differences. One is that the concentrations of solution are variable while the composition of compounds is constant. Another is that the percentages can be calculated using volumes as well as weights, or even both together.

One way of expressing concentrations, with which you might be familiar, is by **volume percent**. Another is by **weight percent**. Still another is a hybrid called **weight/volume percent**.

**Volume percent** is usually used when the solution is made by mixing two liquids.

For example, rubbing alcohol is generally 70% by volume isopropyl alcohol. That means that 100 ml of solution contains 70 ml of isopropyl alcohol. That also means that a liter (or 1000 ml) of this solution has 700 ml of isopropyl alcohol plus enough water to bring it up a total volume of 1 liter, or 1000 ml.

$$\text{Volume percent} = \frac{\text{Volume of solute}}{\text{Volume of solution}} \times 100\%$$

**Weight Percent**, another similar way of expressing the concentration of a solution is to express it in weight percent (or mass percent).

$$\text{weight percent} = \frac{\text{weight of solute}}{\text{weight of solution}} \times 100\%$$

As an example, let us consider a 12% by weight sodium chloride solution. Such a solution would have 12 grams of sodium chloride for every 100 grams of solution. To make such a solution, you could weigh out 12 grams of sodium chloride, and then add 88 grams of water, so that the total mass for the solution is 100 grams. Since mass (unlike volume) is conserved, the masses of the components of the solution, the solute and the solvent, will add up to the total mass of the solution. 12 % NaCl solution = 12 g NaCl , 100 g solution

$$(12 \text{ g NaCl} + 88 \text{ g water}) = 12\% \text{ NaCl solution}$$

**Question:**

What is the weight percent of glucose in a solution made by dissolving 4.6 g of glucose in 145.2 g of water?

**Analysis:**

To get weight percent we need the weight of the solute and the total weight of the solution.

**Determine total weight of solution:**

4.6		g glucose
+	145.2	g water
149.8 g		solution

**Calculate percent:**

$$\text{Weight \% glucose} = \frac{4.6 \text{ g glucose}}{149.8 \text{ g solution}} \times 100 = 3.1\% \text{ glucose}$$

**Weight/Volume Percent**, another variation on percentage concentration is weight/volume percent or mass/volume percent. This variation measures the amount of solute in grams but measures the amount of solution in milliliters. An example would be a 5 % ( w/v) NaCl solution. It contains 5 g of NaCl for every 100. mL of solution.

$$\text{Weight /Volume percent} = \frac{\text{Weight of solute (g)}}{\text{Volume of solution(ml)}} \times 100\%$$

Because of the different units in the numerator and denominator, this type of concentration is not a true percentage. It is used as a quick and easy concentration unit because volumes are easier to measure than weights and because the density of dilute solutions is generally close to 1 g/mL. Thus, the volume of a solution in mL is very nearly numerically equal to the mass of the solution in grams.

**When the type of percent is not stated, it is understood that dilutions of (1) dry ingredient in a dry preparation are percent W/W, (2) dry ingredients in a liquid are percent W/V, and (3) a liquid in a liquid is percent V/V.**

**Molarity**

*Molarity is the number of moles of solute dissolved in one liter of solution. The units, therefore are moles per liter, specifically it's moles of solute per liter of solution.*

$$\text{Molarity} = \frac{\text{moles of solute}}{\text{liters of solution}}$$

Rather than writing out moles per liter, these units are abbreviated as M. You must be very careful to distinguish between moles and molarity. "Moles" measures the amount or quantity of material you have; "molarity" measures the concentration of that material. So when you're given a problem or some information that says the concentration of the solution is 0.1 M that means that it has 0.1 mole for every liter of solution; it does not mean that it is 0.1 moles.

### Molality

The molal concentration, *m*, is the number of moles of the solute contained in **one kilogram of solvent**.

### Normality

When we need to compare solutions based on concentration of specific ions or the amount of charge that the ions have, a different measure of concentration can be very useful. It is called normality. The normal concentration, *N*, of a solution expresses the number of milliequivalents (mEq) of solute contained in 1 ml of solution, or the number of equivalents of solute contained in 1 L of solution.

Normality is the only concentration unit that is reaction dependent, it depends on the reaction capacity (or the number of accessible protons for acids and bases, or the number of electrons gained or lost for electron transfer reactions).

The quantities of electrolytes are usually expressed in Eq, because of the electrical properties of ions. An equivalent is the weight of a substance that supplies one unit of charge. An equivalent weight is the weight, in g, of an atom or radical divided by the valence ( $\eta$ ) of the atom or radical.

$$N = \frac{\text{Number of Equivalent (Eq)}}{\text{volume (L)}}$$

$$\text{Eq} = \frac{\text{Mass}}{\text{Equivalent weight (Ew)}}$$

$$\text{Ew} = \frac{\text{Molecular weight (MWt)}}{\eta}$$

$$N = M \times \text{Valency}$$

**Examples:**

- 1 M sulfuric acid ( $H_2SO_4$ ) is 2 N for acid-base reactions because each mole of sulfuric acid provides 2 moles of  $H^+$  ions.
- 1 M sulfuric acid is 1 N for sulfate precipitation (ppt reaction), since 1 mole of sulfuric acid provides 1 mole of sulfate ions.
- 36.5 grams of hydrochloric acid (HCl) is a 1 N (one normal) solution of HCl.

Since hydrochloric acid is a strong acid that dissociates completely in water, a 1 N solution of HCl would also be 1 N for  $H^+$  or  $Cl^-$  ions for acid-base reactions.

**Least Measurable Quantities (Volume/Weight):**

- **MEASUREMENT OF VOLUME:** Common instruments for the pharmaceutical measurement of volume range from micropipets and burettes used in analytic procedures to large, industrial-size calibrated vessels. The selection of measuring instrument should be based on the level of precision required.

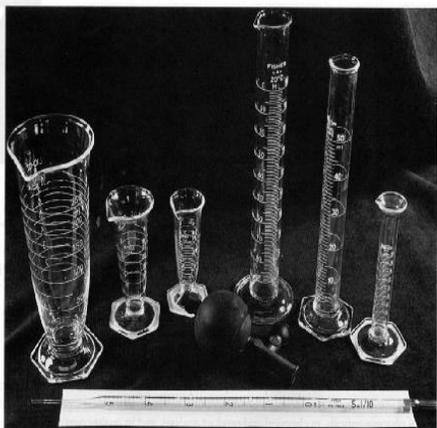


FIGURE 3.1 Examples of conical and cylindrical graduates, a pipet, and a pipet-filling bulb for volumetric measurement.

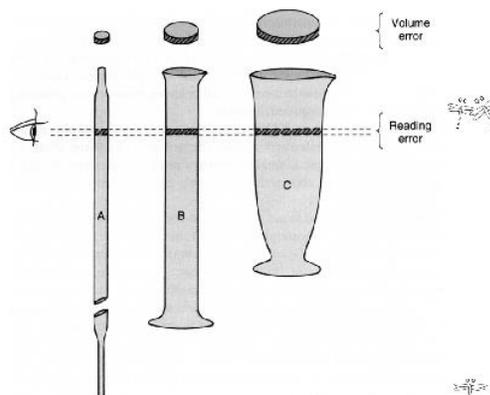


FIGURE 3.2 Volume error differentials due to instrument diameters: (A), volumetric pipet; (B), cylindrical graduate; and (C), conical graduate.

As a general rule, it is best to select the graduate with a capacity equal to or just exceeding the volume to be measured. Measurement of small volumes in large graduates tend to increase the size of error. The design of volumetric apparatus is an important factor in measurement of accuracy. The narrower the bore of the chamber, the lesser the error in reading the meniscus and the more accurate the measurement.

- **MEASUREMENT OF WEIGHT:** The selection of implements:
  1. balances, and scales for pharmaceutical measurement depends on the task at hand,
  2. highly sensitive electronic analytic balances in performing assay tests
  3. prescription balances in extemporaneous compounding procedures
  4. large capacity scales in the industrial manufacturing and production of pharmaceutical agents.
- Each instrument used must meet established standards for sensitivity, accuracy, and capacity

Class A balances (Fig. 3.3) are designed for small scale compounding and have sensitivity requirements of (6) mg or less with no load and with load of (10) gm. To avoid errors of greater than 5% when using this balance, the pharmacist should not weigh less than 120 mg of material (i.e., a 5% error in a weighing of 120 mg = 6 mg) most commercially available class A balances have a **maximum capacity of 120 gm.**



**FIGURE 3.3** Torbal torsion balance and Chaus electronic balance. (Courtesy of Total Pharmacy Supply, Inc.)

The term sensitivity requirement is defined as the load that will cause a change of one division on the index plate of the balance.

For greater accuracy than class a balances, many pharmacies utilize high precision electronic analytical balances to weigh very small quantities. Many of these balances are capable of weighing accurately 0.1 mg, are self-calibrating, and are equipped with convenient digital readout features. The usual maximum capacities for the balances of this precision range from about 60 gm-210 gm depending upon the model (Fig. 3.4).



**FIGURE 3.4** Sartorius BasicLite analytical balance. (Courtesy of Sartorius Corporation.)

**Weighing by the aliquot method:**

The aliquot method of weighing is a method by which small quantities of a substance may be obtained within the desired degree of accuracy by weighing a larger than need portion of the substance, diluting it with an inert material, and then weighing a portion (aliquot) of the mixture calculated to contain the desired amount of the needed substance.

**Least weighable quantity method of weighing**

This method may be used as an alternative to the aliquot method of weighing to obtain small quantities of a drug substance where we can calculate the amount of diluents according to the next equation:

Amount of drug need/drug-diluent mixture to be weighed = total drug substance weighed / total amount of drug-diluent mixture prepared

- **Weighing by the aliquot method steps:**

Example (1): *If 5 milligrams of a drug substance are needed to fill a prescription, explain how you would obtain this amount of drug with an accuracy of  $\pm 5\%$  using a balance with a sensitivity requirement of 6 milligrams. Use lactose as the diluent.*

- **Preliminary step:**


CALCULATIONS CAPSULE

### Weighing Accuracy

- The sensitivity requirement (SR) of a balance must be known or determined. An SR of 6 mg is usual.
- An error in weighing of  $\pm 5\%$  or less is acceptable.
- The smallest quantity that should be weighed on a prescription balance is determined by the equation:

$$\frac{100\% \times \text{Sensitivity Requirement (mg)}}{\text{Acceptable Error (\%)}} = \text{Smallest Quantity (mg)}$$

That quantity is usually about 120 mg.

- To weigh smaller quantities, an electronic balance or the aliquot method of weighing should be used.

**– Step 1. Select a multiple of the desired quantity that can be weighed with the required precision.**

If the quantity of a required substance is less than the minimum weighable amount, select a "multiple" of the required quantity that will yield an amount equal to or greater than the minimum weighable amount. [A larger-than-necessary multiple may be used to exceed the minimum accuracy desired.]

The balance in the example in the preliminary step is used and if 5 mg of a drug substance is required on a prescription, then a quantity at least 24 times {the "multiple"} the desired amount (  $\frac{120}{5}=24x$ , must be weighed for the desired accuracy.

- (If a larger multiple is used, say 30, and 150 mg of the substance is weighed [5 mg X 30], then a weighing error of only 4% would result.)

**– Step 2. Dilute the drug substance with a calculated quantity of inert diluent such that a predetermined quantity of the drug-diluent mixture will contain the desired quantity of drug.**

**-Step 3. Measure the aliquot of the dilution that contains the quantity originally desired.**

The amount of inert diluent to use is determined by the fact that the aliquot portion of the drug-diluent mixture weighed in Step 3 must be equal to or greater than the minimum weighable quantity previously determined.

- By multiplying the amount of the aliquot portion to weigh in Step 3 by the multiple selected in Step 1, the total quantity of the mixture to prepare is determined.

Example: according to the preliminary step, 120 milligrams or more must be weighed for the desired accuracy. If we decide on 120 mg for the aliquot portion in Step 3, and multiply it by the multiple selected in Step 1 (i.e., 24), we arrive at 2880 mg for the total quantity of the drug-diluent mixture to prepare.

- Subtracting the 120mg of drug weighed in Step 1, we must add 2,760 mg of diluent to prepare the 2880 mg of drug-diluent mixture.

The total amount of diluent to use may then be determined through the calculation of the following proportion:

$$\frac{5 \text{ mg (Amount of drug need)}}{120 \text{ mg (Drug-diluent mixture to be weighed)}} = \frac{120 \text{ mg (Total drug substance weighed)}}{X \text{ mg (Total amount of drug-diluent mixture prepared)}}$$

x = 2880 milligrams (mg) of the drug-diluent mixture to prepare. Hence, 2880 mg — 120 mg = 2760mg of diluent (lactose) to use, answer.

•Each weighing, including that of the drug substance, the diluent, and the drug-diluent mixture, must be determined to be equal to or greater than the least weighable quantity as determined for the balance used and accuracy desired.

*Example (2) : a torsion prescription balance has a sensitivity requirement of 6 milligrams. Explain how you would weigh 4 milligrams of atropine sulfate with an accuracy of  $\pm 5\%$ , using lactose as the diluent.*

–  $\because$  6 milligrams is the potential balance error, 120 milligrams is the smallest amount that should be weighed to achieve the required precision.

– If 120 milligrams, or 30 times the desired amount of atropine sulfates, is chosen as the multiple quantity to be weighed in Step 1 (  $120/4 = 30x$  )

– if 150 milligrams is set as the aliquot to be weighed in Step 3, then:

1. Weigh  $30 \times 4$  mg, or 120 mg of atropine sulfate

2. Dilute with 4380 mg of lactose to make 4500 (  $150 \times 30$  ) mg of dilution

3. Weigh  $1/30$  of dilution, or 150 mg of dilution, which will contain 4 mg of atropine sulfate, answer.

$$\frac{4 \text{ mg (Amount of drug need)}}{150 \text{ mg (Drug-diluent mixture to be weighed)}} = \frac{120 \text{ mg (Total drug substance weighed)}}{X \text{ mg (Total amount of drug-diluent mixture prepared)}}$$

In this example, the weight of the aliquot was arbitrarily set as 150 mg, which exceeds the weight of the multiple quantity, as it preferably should.

• If 120 mg had been set as the aliquot, the multiple quantity should have been diluted with 3,480 mg of lactose to get 3,600 mg of dilution, and the aliquot of 120 mg, would have contained 4 mg of atropine sulfate.

• if 200 mg had been set as the aliquot, the multiple quantity of atropine sulfate should have been diluted with 5,880 mg of lactose to get 6,000 mg of dilution.

### Measuring Volume by the aliquot Method

• may be used when relatively small volumes must be measured with great precision:

– Step 1. Select a multiple of the desired quantity that can be measured with the required precision.

– Step 2. Dilute the multiple quantity with a compatible diluent (usually a solvent for the liquid to be measured) to an amount evenly divisible by the multiple selected.

– Step 3. Measure the aliquot of the dilution that contains the quantity originally desired.

*Example (4): A prescription calls for 0.5 milliliter of hydrochloric acid. Using a 10-milliliter graduate calibrated from 2 to 10 milliliters in 1 -milliliter divisions, explain how you would obtain the desired quantity of hydrochloric acid by the aliquot method.*

• If 4 is chosen as the multiple (  $2/0.5=4x$  ), and if 2 milliliters (mL) is set as the volume of the aliquot, then:

1. Measure  $4 \times 0.5$  mL, or 2 mL of the acid

2. Dilute with 6 mL of water

3. to make 8 mL of dilution
4. Measure 1/4 of dilution, or 2 mL of dilution, which will contain 0.5 mL of hydrochloric acid, answer.

*Example (5): A prescription calls for 0.2 mL of clove oil. Using a 5-mL graduate calibrated in units from 1-5 ml, how would you obtain the required amount of clove oil using the aliquot method and alcohol as the diluent?*

- If 5 is chosen as the multiple, then:
  1. Measure 5 X 0.2 mL, or 1.0 mL of clove oil
  2. Dilute with 4.0 mL of alcohol
  3. to make 5.0 mL of dilution
  4. Measure 1/5 of the dilution, or 1.0 mL, which contains 0.2 mL of clove oil, answer.

### **PERCENTAGE OF ERROR:**

*Because measurements are never absolutely accurate, it is important for the pharmacist to recognize the limitations of the instruments used and the magnitude of the errors that may be incurred.*

- *When a pharmacist measures a volume of liquid or weighs a material, two quantities become important:*

1. *the apparent weight or volume measured*
2. *the possible excess or deficiency in the actual quantity obtained.*

- *Percentage of error may be defined as the maximum potential error multiplied by 100 and divided by the quantity desired.*

- *The calculation may be formulated as follows:*

$$\frac{\text{Error} \times 100\%}{\text{Quantity desired}} = \text{Percentage of error}$$

*Example(5) : Using a graduated cylinder, a pharmacist measured 30 milliliters of a liquid. On subsequent examination, using a narrow-gauge burette, it was determined that the pharmacist had actually measured 32 milliliters. What was the **percentage of error** in the original measurement?*

*– 32 milliliters - 30 milliliters = 2 milliliters, the volume of error*

$$\frac{2 \text{ mL} \times 100\%}{30 \text{ mL}} = 6.7\%, \text{ answer.}$$

*Example (6): A prescription calls for 800 milligrams of a substance. After weighing this amount on a balance, the pharmacist decides to check by weighing it again on a more sensitive balance, which registers only 750 milligrams. Because the first weighing was 50 milligrams short of the desired amount, what was the percentage of error?*

$$\frac{50 \times 100\%}{800} = 6.25\%, \text{ answer.}$$

### **Reducing/Enlarging Formulas:**

Most of the preparations made in a pharmacy are from proven formulas that have been tested and are listed in the United States Pharmacopeia/National Formulary (USP/NF) as official formulas. These formulas list the amount of each ingredient needed to make a certain amount of the preparation. At times, it is necessary to reduce or enlarge a formula to satisfy the needs of your pharmacy.

### **1- Ratio and Proportion Method**

The formula:

$$\text{IF } \frac{\text{Amount of each ingredient in the official formula}}{\text{Total quantity of the official formula}} = \text{THEN } \frac{\text{*Amount of each ingredient needed}}{\text{Total quantity desired}}$$

\*NOTE: Most of the time, the unknown factor will be the “Amount of each ingredient needed.”

**Sample Problem:** Using the official formula below, calculate the amount of each ingredient needed to make 240 ml of Peppermint Spirit.

Peppermint Spirit

Peppermint Oil..... 100 ml

Peppermint Powder.....10 g

Alcohol.....qs ad..... 1000 ml

(1) Solve first for the amount of peppermint oil needed:

IF THEN

$$\frac{100 \text{ ml Peppermint oil}}{1000 \text{ ml spirit}} = \frac{X \text{ ml peppermint oil}}{240 \text{ ml spirit}}$$

$$100 \text{ ml Peppermint oil} = X \text{ ml peppermint oil}$$

$$X = 24 \text{ ml of peppermint oil}$$

(2) To solve for the amount of peppermint powder needed:

IF THEN

$$\frac{10 \text{ g peppermint powder}}{1000 \text{ ml of spirit}} = \frac{X \text{ g peppermint powder}}{240 \text{ ml of spirit}}$$

$$10 \text{ g peppermint powder} = X \text{ g peppermint powder}$$

$$X = 2.4 \text{ g of Peppermint powder}$$

c. Knowing that qs ad means to “add a sufficient quantity up to,” take 2.4 g of peppermint powder, add 24 ml of peppermint oil, and add as much alcohol as is necessary to make 240 milliliters. The final product will be Peppermint Spirit.

### **2- Dilution Factor Method**

The dilution factor method is the easiest and therefore the most widely used method for reducing or enlarging formulas.

Find the dilution factor:

$$\text{Dilution factor} = \frac{\text{Total quantity desired}}{\text{Total quantity of official formula}}$$

Note: The “Total Quantity Desired” and the “Total Quantity of Official Formula” must have the same units so the units will cancel and yield a dilution factor without units.

Use dilution factor in formula:

$$\text{Dilution factor} * \text{amount of ingredient in official formula} = \text{amount of each ingredient needed}$$

**Sample Problem:** Use the official formula below to calculate how much of each ingredient would be needed to make 120 ml of Cocoa Syrup.

Cocoa Syrup

Cocoa.....	180 g
Sucrose.....	600 g
Liquid glucose.....	180 ml
Glycerin.....	50 ml
Sodium chloride.....	2 g
Vanillin.....	0.2 g
Sodium benzoate.....	1 g
Pure water .....	qs ad ..... 1000 ml

(1) The first step is to find the dilution factor:

$120 \text{ ml} / 1000 \text{ ml} = \text{dilution factor}$

NOTE: The units, by being the same, cancel.

$0.12 = \text{dilution factor}$

(2) The second step is to multiply the dilution factor times the amount of each ingredient in the original formula:

dilution X Factor	Amount of Ingredient in Official Formula	=	Amount of Each Ingredient Needed
----------------------	---	---	-------------------------------------

$0.12 \times 180 \text{ g} = 21.6 \text{ g of cocoa}$

$0.12 \times 600 \text{ g} = 72.0 \text{ g of sucrose}$

$0.12 \times 180 \text{ g} = 21.6 \text{ g of liquid glucose}$

$0.12 \times 50 \text{ ml} = 6.0 \text{ ml of glycerin}$

$0.12 \times 2 \text{ g} = 0.24 \text{ g of NaCl}$

$0.12 \times 0.2 \text{ g} = 0.024 \text{ g of vanillin}$

$0.12 \times 1.0 \text{ g} = 0.12 \text{ g of sodium benzoate}$

$0.12 \times \text{qs } 1,000 \text{ ml} = 120 \text{ ml with pure water}$

### **Stock Solutions:**

Pharmacy personnel will often go to a stock solution to obtain the amount of active ingredient that is needed to make a preparation. This is especially true if the amount required is so small that it cannot be accurately weighed on a torsion balance. It is easier to measure an amount of stock solution than to set up a balance, weigh the ingredients, and compound the entire product. The use of stock preparations is an important aspect of pharmacy.

**Formulas: In order for these formulas to work:**

- Volumes and weights must be expressed in the same units.
- Concentrations must be expressed in the same units.
- Formula:  $V C = V_1 C_1$

Where: V = Volume of stock preparation

C = Concentration of stock preparation

V<sub>1</sub> = Volume of desired preparation

C<sub>1</sub> = Concentration of desired preparation

- Formula:  $W C = W_1 C_1$

Where: W = Weight of stock preparation

C = Concentration of stock preparation

W<sub>1</sub> = Weight of desired preparation

C<sub>1</sub> = Concentration of desired preparation

Example: A pharmacist is preparing an ophthalmic decongestant solution in batch form. Each of three bottles will contain 15 mL. The preservative to be incorporated is 0.01% benzalkonium chloride (BAK). The pharmacist has a stock solution containing 17% BAK. How much of this stock solution would be required for the three bottles?

$$\begin{array}{rcl}
 15 \times 3 & = & 45 \text{ mL} \\
 C_1 * V_1 = C_2 & * & V_2 \\
 17\% * V_1 = 0.01\% & * & 45 \\
 x & = & 0.026\text{mL}
 \end{array}$$

**Specific Gravity in Weighing/Measuring:**

Specific gravity often becomes a part of the solution to a pharmaceutical calculation. Hence, the main use of specific gravity is to solve for *a liquid's volume when the weight of the liquid is known*. Because of the difficulty which may be encountered in trying to weigh a liquid, it is often advantageous to calculate the liquid's volume and measure it in a graduate as opposed to weighing it.

*It is the ratio of weight of a substance in air at 25° to that of the weight of an equal volume of water at the same temperature.* Expressed without units.

At 25°C and 1 atmosphere of pressure, one milliliter of distilled water weighs one gram. Therefore, the specific gravity of water is established as one.

**Specific gravity = Weight of the substance/Weight of an equal volume of water**

**Example:** If 54.96 mL of an oil weighs 52.78 g, what is the specific gravity of that oil?

$$\text{Specific Gravity} = \frac{52.78 \text{ g oil}}{54.96 \text{ g water}}$$

$$\text{S.G} = 0.9603$$

*Because the volume of the liquid in question is assumed to be the same as volume as water and one milliliter of water weighs one gram:*

**Specific gravity = Number of grams of the substance/ Number of milliliters of the substance**

- Specific gravity has no units. Because specific gravity has no units, only the numbers must be placed in the formula providing the units of weight and volume are grams and milliliters
- It's important to remember that specific gravity is *a factor* that expresses how much *heavier or lighter* a substance is than water ,i.e. Substances that have a specific gravity less than 1 are lighter than water and Substances that have a specific gravity greater than 1 are heavier than water .

**Example:** A pharmacist receives a prescription for 120 mL of a 3% w/v Hydrochloric Acid solution. The density of concentrated hydrochloric acid (37% v/v) is 1.18 g/mL. How many milliliters of the concentrated acid would be required for the Rx?

$$3\% = 0.03$$

$$0.03 \times 120 \text{ mL} = 3.6 \text{ g required}$$

$$\text{Volume} = 3.6 \text{ g} / 1.18 \text{ g/mL} = 3.05 \text{ mL}$$

$$37\% = 0.37 \quad , \quad 3.05 \text{ mL} / 0.37 = 8.24 \text{ ml}$$

**Example:** What is the weight in grams of 240 milliliters of light liquid petrolatum having a specific gravity of 0.81?

$$g = \text{sp gr} \times \text{ml}$$

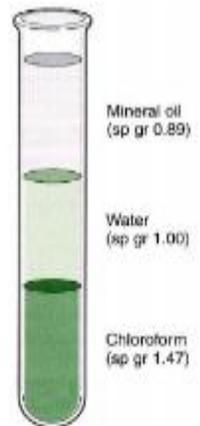
$$g = 0.81 \times 240$$

$$g = 194.4 \text{ (answer)}$$

240 milliliters of light liquid petrolatum weighs 194.4 grams.

**TABLE 5.1 SOME REPRESENTATIVE SPECIFIC GRAVITIES AT 25°C**

AGENT	SP GR
Ether (at 20°C)	0.71
Isopropyl alcohol	0.78
Acetone	0.79
Alcohol	0.81
Liquid petrolatum	0.87
Peppermint oil	0.90
Olive oil	0.91
Peanut oil	0.92
Cod liver oil	0.92
Castor oil	0.96
<b>Water</b>	<b>1.00</b>
Propylene glycol	1.03
Clove oil	1.04
Liquefied phenol	1.07
Polysorbate 80	1.08
Polyethylene glycol 400	1.13
Glycerin	1.25
Syrup	1.31
Hydrochloric acid	1.37
Nitric acid	1.42
Chloroform	1.47
Nitroglycerin	1.59
Phosphoric acid	1.70
Mercury	13.6



**Figure 1**

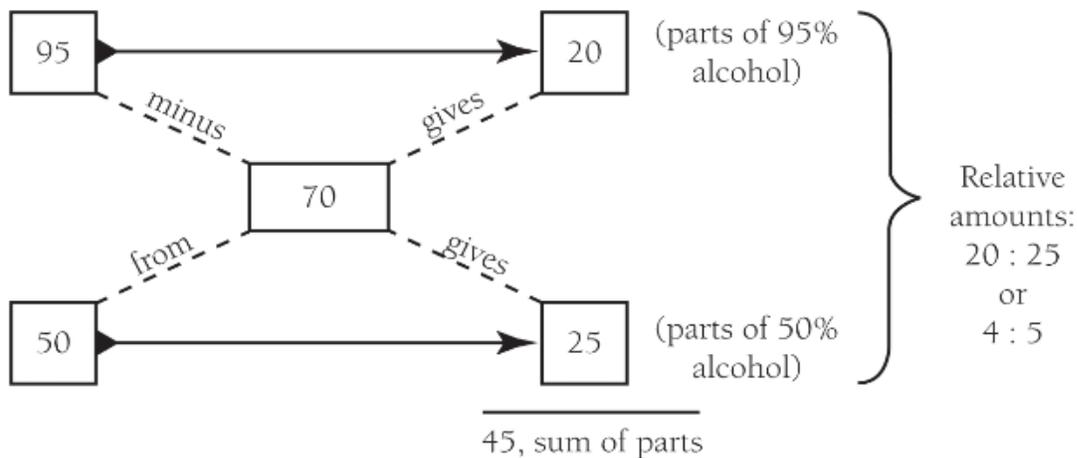
**Alligation**

Alligation is a method used to solve problems that involve mixing two products of different strengths to form a product having a desired intermediate strength. Alligation is used to calculate:

- The amount of diluent that must be added to a given amount of higher strength preparation to make a desired lower strength.
- The amounts of active ingredient which must be added to a given amount of lower strength preparation to make a higher strength.
- The amount of higher and lower strength preparations that must be combined to make a desired amount of an intermediate strength.

**Example**

In what proportion should alcohols of 95% and 50% strengths be mixed to make 70% alcohol?



Note that the difference between the strength of the stronger component (95%) and the desired strength (70%) indicates the number of parts of the weaker to be used (20 parts), and the difference between the desired strength (70%) and the strength of the weaker component (50%) indicates the number of parts of the stronger to be used (25 parts).

Q: In what quantities could 50% dextrose in water be mixed with a 5% dextrose in water to obtain 900 mL of 15% dextrose in water?

**Units to Weight Conversions:**

A Rx order calls for 150,000 units of nystatin per gram of ointment with 60 grams to be dispensed. How much nystatin would be weighed? (4400 USP Nystatin units/mg)

$$150,000 \text{ u/g} \times 60 \text{ g} = 9,000,000 \text{ units needed}$$

$$9,000,000 / 4400 \text{ u/mg} = 2.045 \text{ g required}$$

**POST LAB**

**STUDENT NAME:**.....**I.D #**.....

**Q1:** A pharmacist prepared a suspension containing 5 million units of penicillin per 10 milliliters. How many units of penicillin will 1/4 milliliter of the suspension contain?

**Q2:** Actifed Syrup is indicated for the symptomatic relief of upper respiratory congestion due to allergies. Each 5 milliliters of the yellow syrup contains Pseudoephedrine 30mg, Triprolidine 1.25mg:

(a) If there are 473 milliliters in one pint, how many milligrams of triprolidine are in one pint of the Actifed Syrup?

(b)The manufacturer suggests a dosage regimen of 0.938 milligrams Triprolidine every 6 hours for children four to six years old. How many milliliters should a 5 years old child take as a single dose?

**Q3:** Percent means parts of 100. A 5% (W/V) solution contains 5 grams of active ingredient per 100 ml of total solution. With this in mind, calculate how many grams of atropine sulfate are needed to prepare the following prescription?

		gm. or ml.
$\mathcal{R}$	Atropine Sulfate	2%
	Aqua Dist. qs	120
	Mft. Soln.	

**Q4:** How many grams of potassium permanganate are needed to compound the prescription below?

		gm. or ml.
<b>Rx</b>		
<b>KMnO<sub>4</sub></b>	<b>0.02%</b>	
<b>Dist. Water</b>	<b>ad</b>	<b>250</b>
<b>Mft. Soln.</b>		
<b>Sig. Soak fingernail bid</b>		

**Q5:** (a) How many grams of silver nitrate are needed to make the following prescription?

		gm. or ml.
<b>Rx</b>		
<b>Silver Nitrate</b>	<b>qs</b>	
<b>Dist. Water</b>	<b>ad</b>	<b>60</b>
<b>Mft. 1:4000 Soln.</b>		

(b) How many milliliters of a 10% (W/V) silver nitrate solution would you use to get the desired amount?

**Q6:** Use the formula listed below to calculate the amount of each ingredient that should be used to make 60 g of compound senna powder.

Senna.....	180 g	_____g
Glycyrrhiza.....	236 g	_____g
Washed sulfur.....	80 g	_____g
Fennel oil.....	4 g	_____g
Sucrose.....	500 g	_____g

**Q7:** A torsion prescription balance has a sensitivity requirement of 6 mg. explain how you would weigh 2 mg of atropine sulfate with an accuracy of  $\pm 5\%$ , using lactose as the diluents.

**Q8:** Using the formula below, calculate the amount of each ingredient that should be used to make one gallon of calamine lotion.

Calamine..... 8 g \_\_\_\_\_ g  
 Zinc oxide..... 8 g \_\_\_\_\_ g  
 Glycerin..... 2 ml \_\_\_\_\_ ml  
 Avicel R Gel..... 2 g \_\_\_\_\_ g  
 Carboxymethylcellulose..... 2 g \_\_\_\_\_ g  
 Calcium hydroxide soln qs. ....100 ml qs \_\_\_\_\_ ml

**Q9:** a solution of 10 mg% of Ca +2 ions. Express this concentration in terms of milliequivalents per liter.

**Q10:** A prescription balance has sensitivity requirement of 6.5 mg. explain how you would weigh 20 mg of a substance with an error not greater than 2%.

**Q11:** How many mls of a 1% stock solution of a certified red dye should be used in preparing 4000 ml of a mouthwash that is to contain 1: 20,000 w/v of the certified red dye as coloring agent?

**Q12:** If 400 ml of a 20% (w/v) solution are diluted to 2 liters, what will be the percentage strength (w/v)?

**Q13:** what is the concentration in mg/ml, of a solution containing 2 mEq of potassium chloride per ml?

**Q14:** How many grams of coal tar should be added to 3200 g of 5% coal tar ointment to prepare an ointment containing 20% of coal?

## Experiment 2

### Aseptic Processing

#### Objectives:

- To maintain the sterility of a product assembled from sterile components.
- Strict operating conditions so as to prevent microbial contamination.

#### Introduction

Aseptic processing is the process by which a sterile (aseptic) product (typically food or pharmaceutical) is packaged in a sterile container in a way that maintains sterility.

Pharmaceutical sterile processing includes use of clean rooms, bacteria retaining filters, dry or steam heat. Aseptic food preservation methods allow processed food to keep for long periods without preservatives, as long as they are not opened.

Sterile pharmaceuticals are usually packaged in plastic or glass. Together these materials form a tight seal against microbiological organisms, contaminants, and degradation, eliminating the need for refrigeration.

Aseptic processing makes worldwide export and import of new, economical and safe products possible. Certain pharmaceutical products must be sterile such as injections, ophthalmic preparations, irrigations solutions and hemodialysis solutions.

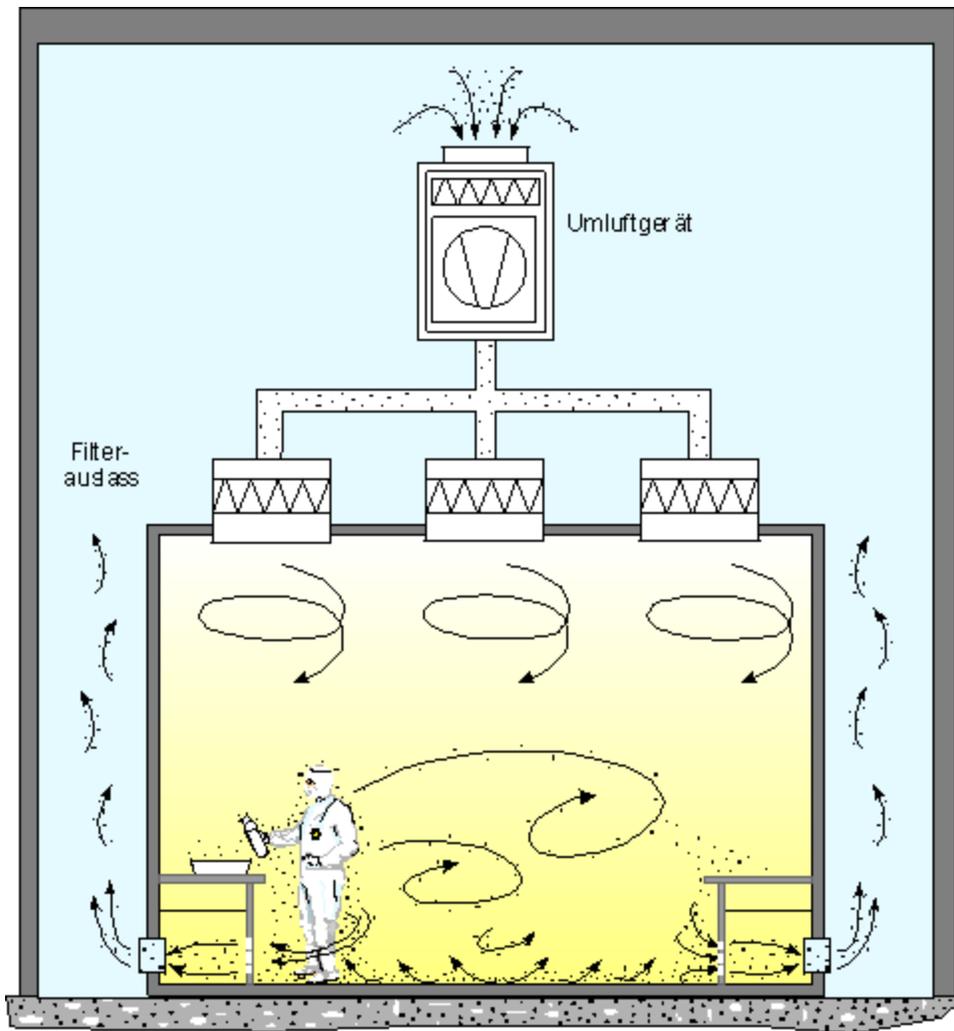
There are two categories of sterile products:

- 1.Those that can be sterilized in final container (terminally sterilized).
- 2.Those that cannot be terminally sterilized and must be aseptically prepared.

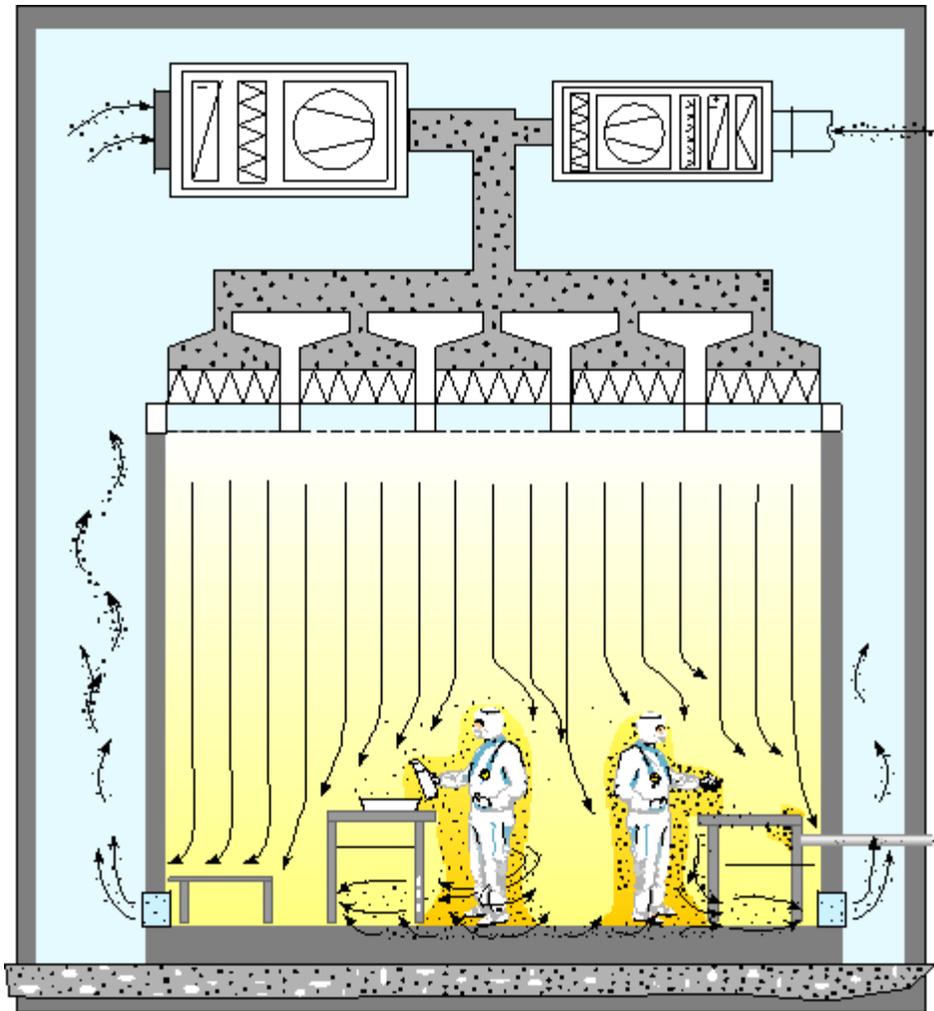
#### Clean Room Technology

A clean room is an environment, typically used in manufacturing or scientific research, with a low level of environmental pollutants such as dust, airborne microbes, aerosol particles, and chemical vapors. More accurately, a cleanroom has a controlled level of contamination that is specified by the number of particles per cubic meter at a specified particle size. To give perspective, the ambient air outside in a typical urban environment contains 35,000,000 particles per cubic meter in the size range 0.5  $\mu\text{m}$  and larger in diameter, corresponding to an ISO 9 cleanroom, while an ISO 1 cleanroom allows no particles in that size range and only 12 particles per cubic meter of 0.3  $\mu\text{m}$  and smaller. In the pharmaceutical industry, clean rooms play a crucial role in the manufacturing of pharmaceutical products which are required to be free from microbial and particulate contamination and required to be protected from moisture. Such pharmaceutical products are manufactured and manipulated in cleanrooms, which are fitted with HEPA and, if required, ULPA filters as well as dehumidifier system.

There are four classes of clean room from least to most clean (D to A) each grade of cleanroom has specifications for viable and non-viable particles. Cleanrooms are classified according to the number and size of particles permitted per volume of air



Air flow pattern for "Turbulent Cleanroom"



Air flow pattern for "Laminar Flow Cleanroom

Cleanrooms maintain particulate-free air through the use of either HEPA or ULPA filters employing laminar or turbulent air flow principles. Laminar, or unidirectional, air flow systems direct filtered air downward or in horizontal direction in a constant stream towards filters located on walls near the cleanroom floor or through raised perforated floor panels to be recirculated. Laminar air flow systems are typically employed across 80% of a cleanroom ceiling to maintain constant air processing. Stainless steel or other non-shedding materials are used to construct laminar air flow filters and hoods to prevent excess particles entering the air. Turbulent or non-unidirectional, air flow uses both laminar air flow hoods and nonspecific velocity filters to keep air in a cleanroom in constant motion, although not all in the same direction. The rough air seeks to trap particles that may be in the air and drive them towards the floor, where they enter filters and leave the cleanroom environment. US FDA and EU have laid down guidelines and limit for microbial contamination which is very stringent to ensure freedom from microbial contamination in pharmaceutical products.

**Personnel contamination of cleanrooms**

In the healthcare and pharmaceutical sectors, control of microorganisms is important, especially microorganisms likely to be deposited into the air stream from skin shedding. Studying cleanroom microflora is of importance for microbiologists and quality control personnel to assess changes in trends. Shifts in the types of microflora may indicate deviations from the “norm” such as resistant strains or problems with cleaning practices. In assessing cleanroom microorganisms, the typical flora are primarily those associated with human skin (Gram-positive cocci), although microorganisms from other sources such as the environment (Gram-positive rods) and water (Gram-negative rods) are also detected, although in lower numbers. Common bacterial genera include *Micrococcus*, *Staphylococcus*, *Corynebacterium*, and *Bacillus*, and fungal genera include *Aspergillus* and *Penicillium*.  
Page Break

## Ocular (ophthalmic) solutions

Ophthalmic solutions are sterile, aqueous solutions used for, among other things, cleansing and rinsing eyeballs. They may contain excipients, which, for example, regulate osmotic pressure, the pH, and viscosity of the preparation. They may also contain preservatives if stored in multiuse packaging [6].

### Examinations of Ophthalmic Drug Forms Properties

Examinations which have to be performed in order to determine the properties may be divided into performed in vitro and in vivo. The former determine sterility, the pH, clarity of solutions, visual assessment, size of the particles, tonicity/osmolality, viscosity, amount of substance, amount of preservative, stability, and in vitro release [7].

### Special considerations

Eye-drops may contain excipients, for example, to adjust the tonicity or the viscosity of the preparation, to adjust or stabilize the pH, to increase the solubility of the active substance, or to stabilize the preparation. These substances do not adversely affect the intended medicinal action or, at the concentrations used, cause undue local irritation.

Aqueous preparations supplied in multi-dose containers contain a suitable antimicrobial preservative in appropriate concentration except when the preparation itself has adequate antimicrobial properties. The antimicrobial preservative chosen must be compatible with the other ingredients of the preparation and must remain effective throughout the period of time during which eye-drops are in use.

If eye-drops are prescribed without antimicrobial preservatives they are supplied wherever possible in **single-dose** containers. Eye-drops intended for use in surgical procedures do not contain antimicrobial preservatives and are supplied in single-dose containers. Eye-drops that are solutions, examined under suitable conditions of visibility, are practically clear and practically free from particles.

Multi-dose preparations are supplied in containers that allow successive drops of the preparation to be administered. The containers contain **at most 10 ml** of the preparation, unless otherwise justified and authorized.

### LABELLING

The label states:

- Where applicable, that the contents are to be used on one occasion only,
- For multi dose preparations, the period after opening the container after which the contents must not be used. **This period does not exceed 4 weeks**, unless otherwise justified and authorized.

**Experimental:****Artificial tears**[8]*Formula*

<i>Sodium Chloride</i>	-----
<i>Hypermellose (HPMC)</i>	0.03g
<i>Boric acid</i>	0.53 g
<i>Borax(sodium tetraborate)</i>	0.05g
<i>Chlorbutanol</i>	0.03g
<i>Water for injection up to</i>	100 mL

**Procedure:**

- 1-Get in advance 0.05g hypromellose and join in appropriate water for injection, dissolve for subsequent use.
- 2-Take respectively sodium chloride 0.55g, chlorbutanol 0.03g, boric acid 0.53g and Borax 0.05g, respectively add appropriate water for injection and mix well.
- 3-Dissolve chlorbutanol with appropriate heating of the distilled water
- 4-Add the mix in step 2 to the chlorbutanol solution and dissolve well at room temperature to mix homogeneously.
- 5-Complete volume with water
- 6-Filter using 0.22 µm filter syringe

Sodium Chloride (Equivalents; Evalue)

E-value for the used ingredients are given below between brackets.

To have an isotonic solution, the preparation should contain an equivalent of approximately 0.9g NaCl in 100 ml of the above formula.

**Boric acid (1g equivalent to 0.52 g of sodium chloride)= so in this formula as if we have 0.2756g of NaCl**

**Borax (1g equivalent to 0.42 g of sodium chloride)**

**Chlorbutanol (1g equivalent to 0.42 g of sodium chloride)**

Perform the calculations and evaluate your preparation with respect to the following criteria (**submit as instructed by your supervisor**):

- 1-Isotonicity. (describe based on the calculation you have reported as being iso or hyper or hypotonic and explain the recommended tonicity for eye solution preparation).
- 2-Measure the pH of your preparation.

- 3-Describe the appearance character of the eye solution (clarity , visible foreign matter, color).
- 4-Analyse the role of the components in your formula and state your recommendation of accepting this product or refusing it based on the characteristics that you have examined (point 1-3); in addition to the appropriateness of the type of materials used in this recipe for hygienic purposes to protect against COVID-19 or dilute viral load.

### Recommended reading

<http://webeye.ophth.uiowa.edu/eyeforum/tutorials/artificial-tears.htm>  
[https://uomustansiriyah.edu.iq/media/lectures/4/4\\_2018\\_02\\_06!11\\_32\\_06\\_AM.pdf](https://uomustansiriyah.edu.iq/media/lectures/4/4_2018_02_06!11_32_06_AM.pdf)  
<http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1520227&blobtype=pdf>

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## Experiment 3

### Pharmaceutical Syrups

#### Pharmaceutical Syrups

Syrups are viscous oral liquids that may contain one or more active ingredients in solution. Sucrose is the primary component in syrups. In non-sugar-based syrups, the formulation is primarily made of cellulose type agents with added sweeteners for taste enhancement. For compounding purposes, and as a quality control test for syrups, it is essential to document the amount of sucrose in the preparation. Addition of sucrose to an aqueous solution renders that solution more viscous. Syrups are known to be viscous liquids. Viscosity of a liquid formulation may serve as an indicator for reproducibility among batches of the product. Added ingredients may potentially modify the syrup viscosity and thus its physical characteristics important for its dose handling [1-5].

#### Preparation of Syrups

Syrup, Pharmacopeial (such as USP) contains 850 gm sucrose and 450 ml of water in each liter of syrup. Although very concentrated, the solution is not saturated. Since 1 gm sucrose dissolves in 0.5 ml water, only 425 ml of water would be required to dissolve 850 gm sucrose. This slight excess of water enhances the syrup's stability over a range of temperatures, permitting cold storage without crystallization.

Syrups should be carefully prepared in clean equipment to prevent contamination. Syrups may be prepared from sugars other than sucrose (glucose, fructose), non-sugar polyols (sorbitol, glycerin, propylene glycol, mannitol), or other non-nutritive artificial sweeteners (aspartame, saccharin) when a reduction in calories or glucogenic properties is desired, as with the diabetic patient. The non-nutritive sweeteners do not impart the characteristic viscosity of syrups and require the addition of viscosity adjusters, such as methylcellulose.

#### Preserving Syrups

Syrup, USP for instance, is protected from bacterial contamination by virtue of its high solute concentration. More dilute syrups are good media for microbial growth and require the addition of preservatives. Industrially formulated syrups often contain ingredients to improve solubility, stability, taste or appearance which also contribute to product preservation. It is necessary, from an economic standpoint, to consider the additive preservative effects of such ingredients as alcohol, glycerin, propylene glycol, and other dissolved solids. Syrup USP, having a specific gravity of 1.313 and a concentration of 85% w/v is a 65% w/w solution. This 65% by weight is the minimum amount of sucrose which will preserve neutral syrup. If one wants to formulate a syrup containing less sucrose, the quantity of alcohol, or other preservatives, may be estimated by considering the *USP Syrup equivalent* and the *free water equivalent*. **One may assume that free water is preserved by 18% alcohol.**

Syrups can be preserved by (a) storage at low temperature, (b) adding preservatives such as glycerin, benzoic acid, sodium benzoate, methyl paraben, or alcohol in the formulation, or (c) by the maintenance of a high concentration of sucrose as a part of the formulation. High sucrose concentrations will usually protect an oral liquid dosage from growth of most microorganisms. A problem arises, however, when pharmacists/pharmaceutical engineer must add other ingredients to syrups that can result in a decrease in

the sucrose concentration. This may cause a loss of the preservative effectiveness of the sucrose. This can be overcome, however, by calculating the quantity of a preservative (such as alcohol) to add to the formula **to maintain the preservative effectiveness** of the final product.

**Example:**

**Formula**

Active drug	5 mL volume occupied
Other drug solids	3 mL volume occupied
Glycerin	15 mL
Sucrose	25 g
Ethanol 95%	q.s.
Purified water q.s.	100 mL

How much alcohol would be required to preserve this prescription? We will use the **free-water method** to calculate the quantity of alcohol required.

Simple syrup contains **85 g sucrose per 100 mL of solution**, which weighs **131.3 g** (specific gravity, 1.313). It takes **46.3 mL of water** to prepare the solution ( $131.3 - 85 = 46.3$ ), and the sucrose occupies a volume of ( $100 - 46.3 = 53.7$ ) 53.7 mL.

1. *Because this solution is preserved, 85 g of sucrose preserves 46.3 mL of water, and 1 g of sucrose preserves 0.54 mL of water. With 25 g of sucrose present, the amount of water preserved is  $25 \times 0.54 = 13.5$  mL*
2. *Because 85 g of sucrose occupies a volume of 53.7 mL, 1 g of sucrose will occupy a volume of 0.63 mL. The volume occupied by the sucrose in this prescription is  $25 \times 0.63 = 15.75$  mL*
3. *The active drug and other solids occupy 8 mL ( $5 + 3$ ) volume.*
4. *Each mL of glycerin can preserve an equivalent quantity of volume ( $2 \times 15 = 30$ ), so 30 mL would be preserved.*
5. *The volume taken care of so far is  $13.5 + 15.75 + 8 + 30 = 67.25$  mL. The quantity of free water remaining is  $100 - 67.25 = 32.75$  mL*
6. *Because it requires about 18% alcohol (dehydrated) to preserve the water,  $0.18 \times 32.75 = 5.9$  mL of alcohol (100%) would be required.*
7. *If 95% ethanol is used,  $5.9/0.95 = 6.21$  mL would be required.*

To prepare the prescription, about 6.21 mL of 95% ethanol can be added with sufficient purified water to make 100 mL of the final solution.

**Experimental:****Part A:****Simple Syrup (Your instructor will inform you which concentration you will prepare):****I-66.7% (w/v): Minimum two students will be preparing this concentration***Formula:**Sucrose*                      667 gm*Purified water up to*    1000 gm

- Regarding the unit, it should be in w/w but due to the nature of the solvent (water) that has a density of 1g/ml and to final dosage form is solution, the final weight= final volume.

Prepare 100 gm syrup**Procedure:**

Heat 40 ml water then add sucrose to them and heat again until clear solution. Filter when it is hot using cotton.

*\*\* Regarding the unit it should be in w/w but due to the nature of the formula (water and sucrose only) and the final dosage form is in solution status; the final weight and volume of the formula will be the same.*

**II-50% (w/v): Minimum two students will be preparing this concentration***Formula:**Sucrose*                      500 gm*Purified water up to*    1000 gmPrepare 100 gm syrup**Procedure:**

Heat 55 ml water then add sucrose to them and heat again until clear solution. Filter when it is hot using cotton.

**III-25% (w/v): Minimum two students will be preparing this concentration***Formula:**Sucrose*                      250 gm*Purified water up to*    1000 gmPrepare 100 gm syrup**Procedure:**

Heat 80 ml water then add sucrose to them and heat again until clear solution. Filter when it is hot using cotton.

**Flavoring Syrup:***Formula*

<i>Orange oil</i>	<i>1 mL</i>
<i>Glycerin</i>	<i>15mL</i>
<i>Sucrose</i>	<i>25 g</i>
<i>Ethanol</i>	<i>q.s.</i>
<i>Purified water up to</i>	<i>100 mL</i>

**Procedure:**

1. Dissolve Orange oil in ethanol.
2. Prepare your syrup by adding sucrose to water and heating until clear solution.
3. Add mixture prepared in step 1 and mix.
4. Add glycerin and mix.
5. Complete volume with water using graduated cylinder.
6. Move the solution into a beaker and add 5 gm of talc with good mixing.
7. Filter using gravity filtration two times.

**Part B:**

To gain an experience with the property of viscosity and develop an understanding of the measurement of this property; create a relative viscosity scale of preparations from Part A (1-3) relevant to the time needed for the syrup to pass through beads.

**First:** You will have a burette filled with beads to a certain height (record the filling height and the relative height with respect to the length of the burette fixed on the stand). Run 5 mL of distilled water and record the time needed for its flow in seconds (**share with your instructor**). Repeat the same using the syrup solutions you have prepared in part A (**share with your instructor**).

**Second:** The times needed to make elution of your simple syrup solution (with different concentration will be reported on the white board by your instructor). You will need to take these readings and construct a calibration curve\* (Y-Axis will be the sucrose concentration and X-Axis will be the time in seconds). Use this calibration curve to estimate the flow time of your flavored syrup. Compare this value with the true value you have obtained for this flavored syrup. Explain the efficiency of using flow rate in correlating sucrose concentration and thus its viscosity. **Submit these results in a report format as indicated by your instructor and analyze the role of the components in simple syrup and flavored syrup formula.**

\* The time needed for test solutions to travel through the beads will be shown in this Table

Concentration of Syrups(% w/w)	Time (sec.) (Avg. value±S.D.)
0% (distilled water)	
25%	
50%	
66.7%	

## Experiment 4

### Pharmaceutical Dispersed Systems: (I) Suspensions

#### Pharmaceutical Suspensions

Pharmaceutical liquid suspension is a homogenous dispersion of poorly soluble drug particles (solid) in a certain dispersion medium (liquid), in which settling behavior of these particles has to be controlled to ensure uniform dosing or stable suspension. Therefore, understanding the interplay between the components of suspension and how their properties can be controlled is a key focus in this session to obtain satisfactory and consistent dispersion of the suspension.

Most solids are difficult to disperse and tend to flocculate after being redispersed and therefore referred to as flocculated suspension. On the other hand, deflocculated suspension can be prepared in which the floccules are not going to form, and solids will have a slower rate of sediment formation and will be prone; however, to more compacted particles or cake formation that will be difficult to redisperse. Therefore, a balance has to be struck to prepare flocculated vs deflocculated suspension/systems.

Chemicals like dispersing, suspending, flocculating or deflocculating agents are added to these solid-liquid mixtures of the suspension to affect factors such as the specific gravity, viscosity and attraction/repulsion forces in these mixtures to induce stability in these systems. The experiment described in this part will be conducted to assess the strategy of adding suspending agents to support the associated dispersion formula and to compare their effectiveness.

#### Preparation of Suspensions

In the case of suspensions, the flow necessary to overcome settling in a satisfactory suspension depends on the mixing equipment and is predicted by Stokes' s law. Thus, to use the Stokes' s law, suspensions are considered as Newtonian fluids if the percentage of solids is below 50%. Mixing equipment uses a mechanical device that moves through the liquid at a given velocity. Dispersing and emulsifying equipment is categorized as "high-shear" mixing equipment. The maximum shear rate with such equipment occurs very close to the mixing impeller. Therefore, the diameter of the impeller and the impeller speed directly influence the power applied by the mixer to the liquid [2]. Raw materials in suspensions can have different purposes and can be wetting agents, salt formation ingredients, buffers, polymers, suspending agents, flocculating agents, electrolytes, antioxidants, poorly soluble Active Product Ingredients, preservatives, coloring, flavoring and sweetener agents, among others. The physical stability of a suspension can be enhanced by controlling the particle size distribution [3]. Uncontrolled changes of drug particle size in a suspension affect the dissolution and absorption of the drug in the patient. Drug substances of finer particle size may be absorbed faster and bigger particles may not be absorbed. Aggregation or crystal growth is evaluated by particle size measurements. Particles are usually very fine (1 -50  $\mu\text{m}$ ). For instance, topical suspensions use less than 25  $\mu\text{m}$  particle size [4].

The particle size of the drug is the most important consideration in the formulation of a suspension, since the sedimentation rate of disperse systems is affected by changes in particle size. Finer particles become interconnected and produce particle aggregation followed by the formation of nonresuspendable

sediment, known as caking of the product. The two main causes of aggregation and caking are energetic bonding and bonding through shared material. A statistical wide distribution of particle sizes gives more compact packing and energetic bonding than narrower distributions. It has been observed that heat treatments can cause agglomeration of particles, not only due to energetic bonding but also by formation of crystal bridges.

### *Uniformity of Oral Suspensions*

Keeping the particles uniformly distributed throughout the dispersion is an important aspect of physical stability in suspensions. Based on Stokes' s law for dilute aspect of physical stability in suspensions. Based on Stokes' s law for dilute suspensions where the particles do not interfere with one another, there are different factors that control the velocity of particle sedimentation in a suspension, for instance, particle diameter, densities of the dispersed phase and the dispersion medium, as well as viscosity of the dispersion medium [5] .

**The factors affecting sedimentation rate of particles are described in Stokes's equation.**

$$v = \frac{2r^2(\rho - \rho_0)g}{9\eta}$$

$v$  = Velocity of spherical particle of radius  $r$  and density  $\rho$ , in a liquid of density  $\rho_0$ , and viscosity  $\eta$

### **Experimental:**

**\*\*Part - A** Many lotions will require the addition of a suspending agent to slow settling.

Prepare the following formula first without any suspending agent (mixture 1) and then with 2 % methylcellulose 1500 as a suspending agent (mixture 2). Pour them both into separate beakers and observe the differences and record your observations.

Sulfur	2.5 g
Camphor	2.5 g
Alcohol	20 ml
Rose water q.s	60 ml

Camphor is difficult to work with as a powder. Therefore dissolve the camphor in the alcohol first and then **triturate** that solution with the sulfur. Gradually with trituration add the rose water. When adding the methylcellulose powder. Mix it with the dry sulfur powder and prepare as before.

**\*\*Part B** - Prepare 40 ml of an **anionic deflocculating(flocculating) agent** which will be used in four of the five suspensions to be made in this part of the laboratory:

Potassium dihydrogen phosphate      2 g  
Purified water q.s                      40ml

Assemble five 25 ml graduated cylinders and number them consecutively. Add 2 g of bismuth subnitrate to each graduated cylinder.

- 1) To the first add sufficient water to make 25 ml of suspension.
- 2) To the second add 10 ml of the anionic flocculating agent solution and enough water to make 25 ml.
- 3) To the third add 10 ml of the anionic flocculating agent solution and sufficient 0.5% methylcellulose solution to make 25 ml.
- 4) To the fourth add 10 ml of the anionic flocculating agent solution and sufficient 1% methylcellulose solution to make 25 ml.
- 5) To the fifth and last add 10 ml of purified water and sufficient 0.5 % methylcellulose solution to make 25 ml.

Cover the graduated cylinders with parafilm. Invert each several time to mix them well and measure and record the height of the suspension (in mls marked on the graduated cylinder) after 15 minutes and 60 minutes. We will assume that the suspension starts at 25mls right after you mix it. Set aside for next week and measure the sediment again in next week's laboratory.

**\*\* Part C** - Obtain four 100 ml graduated cylinders. This experiment will evaluate different suspending agents.

Using a mortar and pestle prepare a suspension of (**and keep them for Part D**):

- 1) 5 gm of Calamine and no suspending agent;
- 2) 5 gm of calamine and 2 grams of acacia,
- 3) 5 gm of calamine and 2 g of sodium carboxymethylcellulose and
- 4) 5 gm of calamine and 1 g of tragacanth.

Transfer the mixture to one of the graduate cylinders, rinse the mortar with additional water and add that to the graduate. Now qs to each mixture to 100 ml. Cover with parafilm and mix. Record the appearance of the suspension and the volume of the sediment at 5 min, 15 min, 45 min. and overnight. Prepare a table with the results and plot the results.

**\*\* Part D**-Create a viscosity scale of the suspensions prepared in part C using viscometer (using different cones and quantities that will be instructed by the TA); to explore the viscosity relevance to the sedimentation rate

### ***Label information***

Store in a cool, dry place.

Should be freshly prepared.

Shelf life ( 2 to 4 weeks)

Shake well before use.

### **Recommended reading**

[https://www.mt.com/de/en/home/applications/L1\\_AutoChem\\_Applications/L2\\_ParticleProcessing/Formulation\\_Flocculation.html](https://www.mt.com/de/en/home/applications/L1_AutoChem_Applications/L2_ParticleProcessing/Formulation_Flocculation.html)

<https://sites.google.com/site/lmcpabd/suspensions>

### **Food for thought**

Sciences are interconnected and can be tailored to serve a certain concept. have a look at the following in-house made sampler (enclosed attachment) and explain its utility for pharmaceutical suspension evaluation (*hint: detail its parts and mechanism of use*).

## Experiment 5

### Preparation of Hand sanitizer (solution vs gel)

#### Hand Hygiene

Healthcare-associated infections (HAIs) challenge healthcare systems worldwide. As healthcare workers' hands are considered the main vector for transmission of pathogens, effective hand hygiene is the single most important action to prevent HAIs.

**Alcohol-based hand-rub (ABHR) solutions** remain the hand hygiene gold standard, but are modified in texture and composition to better meet healthcare workers' preferences. Modifications of the hand hygiene procedure have been proposed targeting both time and technique of hand rub application. Reducing rub-time from 30 to 15 s and simplifying the technique to consist of three rather than six steps yielded encouraging results in terms of microbiological efficacy and higher compliance.

#### Making FDA approved 75% Hand sanitizer solution

Isopropyl alcohol 99.8% 90ml

Glycerol 98% (Glycerine) 1.74ml

Hydrogen peroxide 3% 5ml

Sterile Water 22ml

1- In a beaker, add Glycerin to the Isopropyl alcohol , then

2- Add hydrogen peroxide and mix for 2 minutes then add water.

3-Hand sanitizer solution will be ready after homogenising for 10 minutes and then it can be filled in the indicated container for wiping or spraying applications.

**Making Hand sanitizer Gel**

Glycerol 8 gm (6.7 ml)

Ethanol absolute 20 gm (26 ml)

Carbomer 0.4 gm

Triethanolamine 0.4 gm (7 drops)

Water q.s 50 gm

1. In a beaker, add Carbomer to 22.5 ml distilled water portion wise and mix using magnetic stirring until having uniform dispersion.
2. Add Ethanol and mix then Glycerol.
3. Add Triethanolamine and mix using glass rod.

FOOD FOR THOUGHT FOR PART I an II

**Application to pharmaceutical calculations**

The WHO formula ask for not less than 60% alcohol content in the final content of a hand sanitizer

Isopropyl alcohol 99.8% 240ml pure alcohol

Hydrogen peroxide 3% 13ml

Glycerol 98% 5ml

Water to make a total of 320ml

**Let us prepare 300 mL that contains 70% alcohol ( If you have a strength of 70% Isopropyl alcohol)**

70% of 300 ml=210 pure alcohol

Scaling factor is the  $210/751.5 \times \text{ml} = 0.279$

\*751.5ml is the original amount of pure alcohol in the WHO formula

Hydrogen peroxide 3%  $41.7\text{ml} \times 0.279 = 12 \text{ ml}$

Glycerol 98%  $14.5\text{ml} \times 0.279 = 4 \text{ ml}$

Total solution  $(300 + 12 + 4) = 316 \text{ ml}$  (66% strength of pure alcohol). So the water that will be added will be approximately 90 ml.

Q1 Suggest the formula of the same ingredients if you have a 90% Isopropyl alcohol solution.

**Application of the hand hygiene (alcohol-based)**

The hand hygiene-technique recommended by the WHO was developed to assure complete coverage of hands with Alcohol-based hand-rubs. This includes applying a palmful of alcohol-based hand rub and cover all surfaces of the hands, then rubbing hands until dry. The following Figure is an illustration of the exact steps [\*]:

Apply the simplify procedure of technique through of covering the hands based on own judgement, rubbing the fingertips, that is the most contaminated areas of hands, in the palm of the alternate hand and finally rubbing both thumbs. This is to be performed for 30 s, using 3 ml of hand sanitizer solution and 3ml of hand sanitizer gel.

**Q2 Which product do you think will aid in patient compliance and at the same time will be easier for self-guided method of covering high-touch areas with simplicity and convenience?**

**Q3 Go through the review article entitled as Hand Sanitizers: A Review on Formulation Aspects, Adverse Effects, and Regulations and analyse the role of each component in the above prepared hand sanitizer and mention their potential adverse effects s alcohol-based sanitizer, then suggest an alternative preparation or components.**

Submit Your answers electronically by 29th of October to the TA using word document and including your name and ID number.

[\*] WHO Guidelines on Hand Hygiene in Health Care. ISBN 978 92 4 159790 6.

[https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906\\_eng.pdf;jsessionid=BCF8C85F164A82281C13711F05216F4E?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf;jsessionid=BCF8C85F164A82281C13711F05216F4E?sequence=1).

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2. Reepmeyer , J. C. , Revelle , L. K. , and Vidavsky , I. ( 1998 ), Detection of clobetasol propionate as an undeclared steroid in zinc pyrithione formulations by high - performance liquid chromatography with rapid - scanning ultraviolet spectroscopy and mass spectrometry . *Journal of Chromatography A* , Vol. 828 , Number 1 , 18 December 1998, pp. 239 – 246(8) .
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4. USA Department of Health and Human Services: Food and Drug Administration (FDA) . Guides to inspections. Available at [http://www.fda.gov/ora/Inspect\\_ref/igs/iglist.html](http://www.fda.gov/ora/Inspect_ref/igs/iglist.html)
5. Sinko , P. J. Martin ' s *Physical Pharmacy and Pharmaceutical Sciences* , Lippincott Williams & Wilkins , Baltimore, MD., 2005, pp. 795. 47.

## Experiment 6

### Preparation and Evaluation of Cream: In vitro occlusion efficiency test (skin hydrating effect)

#### OBJECTIVE:

1. To appraise the purpose of the skin cream-topical- ingredients
2. To learn the method of preparing a simple skin cream

#### INTRODUCTION:

The function of a skin cream is to protect the skin relatively from invasive environmental conditions. A skin cream should aid the skin in carrying out its normal functions that is restoring moisture to dry skin, allowing the elimination of waste matter through the pores, and the cooling of the body by evaporation of water (perspiration), thus aiding in the maintenance of the normal body temperature. If the cream clogs the pores of the skin with heavy, insoluble, inert material, it results in a thick sticky coating on the skin and prevents sufficient normal skin function, being detrimental to health (**risk of maceration**).

Skin creams contain a variety of ingredients that range from common, such as mineral oil, to the exotic, such as placenta extract. Some skin creams may contain small amounts of vitamins or other “nutrients”.

Skin creams contain ingredients for adding body, improving texture, emulsifying the oil and water components, raising the melting point, improving the spreadability, improving the odor, softening the skin, and providing various **medicinal properties**-mainly local (**examples**).

#### Common ingredients for Preparing Creams

##### 1. Water

Water is an important part of creams. Usually water from the tap is not good enough, because creams made by this kind of water get mildew faster than other creams. Instead you can take mineral water, sterilized water or special waters like rose water.

##### 2. Oil

Oils used in external preparations come from one of three sources:

1. Mineral oil (liquid paraffin) are the most widely used. They are complex mixtures of mainly saturated hydrocarbons.
2. Vegetable oils come from plant sources such as peanut, castor, olive and coconut. Almond oil is very luxury for face creams.
3. Synthetic oils, such as silicone oils, are used as water repellent and occlusive because they are very hydrophobic.

### 3. Thickener

Thickeners are all substances that make a cream out of the liquid (oil and water-**semisolid**). The different thickeners work in different ways. Some are stronger, others weaker. And some are greasy, others give protection to the skin and others have their own healing quality. You can mix several thickeners in one cream. They generally fall (divided) into two main categories; soft and strong thickeners. Examples include:

- Soft paraffin (petrolatum), there are two forms of soft paraffin- yellow and white. The later has been bleached. All of which provide Soft thickening.
- Beeswax, good protection, a film stays on the skin. Strong thickening.
- Cocoa butter, made from cocoa beans, rather greasy. Soft thickening.
- Shea butter, made from the African karite tree. The substance is similar to skin substances. **Heals the skin (mechanism-bonus)**. Soft thickening.
- Wool wax, made from the wool of sheep. Very soft but with healing effects. Soft emulsifier. Soft thickening.
- Cetyl alcohol, a substance similar to skin substances. White and not greasy. Stabilizes emulsions. Very strong thickening.

### 4. Emulsifier

When you want to prepare a cream, you need to combine oily and watery substances. Usually water and oil doesn't connect, they separate as soon as possible. To help both types of substances to connect, you need an emulsifier. The emulsifier connects at one side with the water and at the other side with the oil. This is called an emulsion.

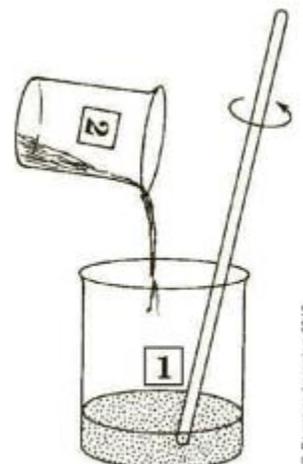
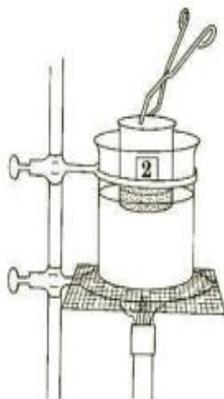
There are different kind of emulsions:

- When there is a lot of oil around some water, it is called water-in-oil-emulsion (W/O).
- When there is a lot of water around some oil, it is called oil-in-water-emulsion (O/W).

Low HLB (hydrophilic lipophilic balance) materials will produce w/o emulsions. Whilst higher HLB surfactants give o/w emulsions.

**Experimental part:****Equipment:**

1. Basin,
2. Glass Rod,
3. 100 ml Erlenmeyer Flask,
4. 25 ml Graduated cylinders,
5. Water Bath,
6. Clamp,
7. Weighing pan.
8. Litmus paper.

**Preparation tips:**

- Maintain temperature at maximum 70 degrees, to prevent decomposition of ingredients.
- Hold the basin steadily to prevent bath water from entering into your basin.
- Make sure to heat the aqueous phase before adding it to the oily phase, in order to prevent clumping and maintain homogeneity of the preparation.
- Continuous stirring is extremely important in maintaining homogeneity of the cream, where the stirring must be in a fast, gentle and circular motion in one direction.

**Cold cream USP:****Formula:**

Spermaceti (Source)	125 gm
White wax	120 gm
Mineral oil	560 gm
Sodium borate	5 gm
Purified water	190 ml

To make about	1000 mg	20 gm
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**Procedure:**

- 1- Reduce the spermaceti and white wax to small pieces. (If needed)
- 2- Melt them on water bath with the mineral oil in basin and continue heating until the temperature of the mixture reaches 70 °C. (Cosmetic ingredients should not be melted over a direct flame or high heat because they may scorch or decompose if they are heated much above the boiling point of water).
- 3-dissolve the sodium borate in water in a small flask at 70 °C.
- 4- Add hot sodium borate solution to the dissolved mixture in basin, stir rapidly until congealed.
- 5-Put in a jar (cream #1).
- 6-Repeat the procedure once without white wax (cream #2), and another without mineral oil (cream #3).

**Vanishing cream B.P:****Formula:**

Stearic acid	150 gm	
White wax	20 gm	
White petrolatum	80 gm	
Triethanolamine	15 ml	
Propylene glycol	80 gm	
Purified water	660 gm	
	-----	-----
To make	1000 g	20 gm

**Procedure:**

- 1- Melt the first three ingredients (oily phase) in basin in water bath (75°C).
- 2- Mix Triethanolamine with propylene glycol and water, heat the mixture in water bath (75°C).
- 3- Pour aqueous solution into oleogenous solution while they are both hot with stirring.
- 4- Stir constantly till congealed.
- 5- Place in a jar (cream #4).
- 6- Repeat the procedure without Triethanolamine (cream #5).

**Part B: Characterization of the Creams:**

For each cream, rub a small amount between your fingers. Note the smoothness, appearance and homogeneity of each, and record your observations. Pay attention to how the properties of the mixtures differ. Test the pH of each cream using pH paper. After you have tested each one, wash your hands.

**Part C: Correlation between In Vitro Occlusion Factor and skin Hydrating Effect.**

A comparison between different cream preparations according to the occlusion factor will be evaluated, and the results were compared with the positive (Vaseline) and negative (blank) controls.

Two petri dishes for each group were given with 50mL of gelatin was cast and chilled (**Wight 1**). Two tablespoons of each of the cream and the petroleum jelly were applied separately in a thin layer on top of the gelatin in each dish, the samples should be close in weight to each other(**Weight 2**).

First: The samples were stored at 32 °C (skin temperature) for 72 h and were weighed (**Weight 3**) to determine the amount of water loss resulting from evaporation through the treated skin. The occlusion factor for tests was calculated according to the following equation:

$$F = \frac{A - B}{A} * 100$$

where, B is the water loss of the skin treated with the formulations and A is the water loss of the skin without a sample (blank reference), *the -ve sign indicates the water loss and have no mathematical meaning*. An occlusion factor of zero indicated no occlusive effect compared with the reference, and 100 was the maximum occlusion factor.

Second: Discuss the results obtained and make a comparison according to the occlusion factor and the weight of the sample.

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**LAB REPORT:**

STUDENT NAME.....I.D #.....

**Characterization of hand cream samples:**

properties	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
pH					
Smoothness					
Homogeneity					
appearance					

- In comparing the properties of the hand creams you produced, ascertain the function of each of the missing ingredients in the hand cream.
  - a. Mineral oil
  - b. Triethanolamine
  - c. Beeswax
- What evidence do you have from your preparation that suggests that the emulsifying agent is necessary component of the hand cream
- Was the pH of all your samples of your hand creams the same? Explain why there was a difference.

## Experiment 7

### Preparation of Ointments

#### OBJECTIVES:

- 1- To be familiar with the different types of ointment bases
- 2- To be familiar with the different methods of ointment preparation

#### INTRODUCTION

Ointments are semisolid preparation intended for application to the skin or mucous membrane. they may be oleaginous e.g., white ointment; they may be entirely free of oleaginous substances e.g., polyethylene glycol ointment, or they may be emulsions of fatty or wax like material containing relatively high proportion of water e.g., hydrophilic ointment.

Ointments can be **prepared** either by mechanical incorporation or by fusion methods. Irrespective of the method employed for the preparation, ointments should be smooth and free from granular or gritty particles. In compounding of ointments, the following general considerations are observed:

- (i) If insoluble substances are to be incorporated in the ointment base then they should be in impalpable-free flowing powder form.
- (ii) For efficient incorporation of insoluble substances they should first be levigated with a little quantity of base to form a smooth cream and then incorporated into the remainder of the base.
- (iii) Water-soluble salts are best incorporated by dissolving them in a small quantity of water and then incorporating in the base.
- (iv) Drugs soluble in ointment bases may also be incorporated by fusion (melting the highest melting point ingredient of the base and mixing the medicament into it). Remaining ingredients are then added and mixed by stirring.

#### Preparation of Ointments by Mechanical Incorporation

This can be achieved by the use of (i) mortar and pestle, (ii) ointment slab and spatula, and (iii) An ointment mill. Mechanical method of incorporation is particularly advantageous when the substance to be incorporated into ointment base must be in a fine state of subdivision (**drawbacks**).

##### a) **Mortar and pestle:**

This method is used to a limited extent in compounding practice particularly when large quantities of liquids are to be incorporated in a base or when exceptionally large quantities of the ointments are to be prepared. Compounding a homogeneous ointment in a mortar and pestle is not as simple as compounding of a powder.

##### b) **Ointment slab:**

In this case both mixing and size reduction of insoluble medicaments are better than the previous method. The powder is first rubbed with a small quantity of the base to form a concentrated ointment base containing a finely divided powder uniformly distributed in it.

The concentrated ointment is then gradually diluted with remaining quantity of the base by rubbing with a spatula. A small quantity of oil or oil-soluble substances can be used as a levigating agent. Large amounts of levigating agents may cause **undue softening** of the finished preparation.

c) **Ointment mill:**

Ointment mills are particularly suitable for large scale manufacture of ointments although small mills are available for laboratory scale ointment preparation. Ointments containing gritty particles are also passed through the ointment mill to ensure further uniformity and smoothness.

Classification of ointment bases (**most common**):

- 1- Hydrocarbon bases (oleogenous).
- 2- Absorption bases (anhydrous).
- 3- Emulsion bases (w/o type)
- 4- Emulsion bases (o/w type)
- 5- Water soluble bases.

**Experimental Part:****Equipments:**

1. Basin
2. Mortar and pestle
3. Spatula
4. Glass rod
5. Graduated cylinder
6. Water bath
7. Cream jar

**\*\*\*Whitefield's ointment B.P, 1980:***Formula*

<i>Salicylic acid(use)</i>	<i>30 gm</i>	
<i>Benzoic acid (use)</i>	<i>60 gm</i>	
<i>Emulsifying wax</i>	<i>50 gm</i>	
<i>White petrolatum</i>	<i>860 gm</i>	
	-----	-----
	<i>1000 gm</i>	<i>20 gm</i>

**Procedure:**

- 1- Take emulsifying wax and white petrolatum in basin in water bath at 70 °C until they melt with continuous mixing with a glass rod.
- 2- Grind salicylic acid and benzoic acid in mortar well then put on a tile and add melted emulsifying ointment on powders portion wise with levigation until it congealed.
- 3- Put in jar.

\*\* Levigation: grinding of solid in the presence of liquid to obtain a paste. Paste is formed by addition of non-solvent molten base. Particle size reduction is then accomplished.

**\*\*\*Zinc oxide ointment U.S.P, 1980:***Formula*

<i>Zinc oxide(used)</i>	<i>200 gm</i>	
<i>Mineral oil</i>	<i>150 gm</i>	
<i>Bees wax</i>	<i>32.5 gm</i>	
<i>White petrolatum</i>	<i>617.5 gm</i>	
	-----	-----
	<i>1000 gm</i>	<i>20 gm</i>

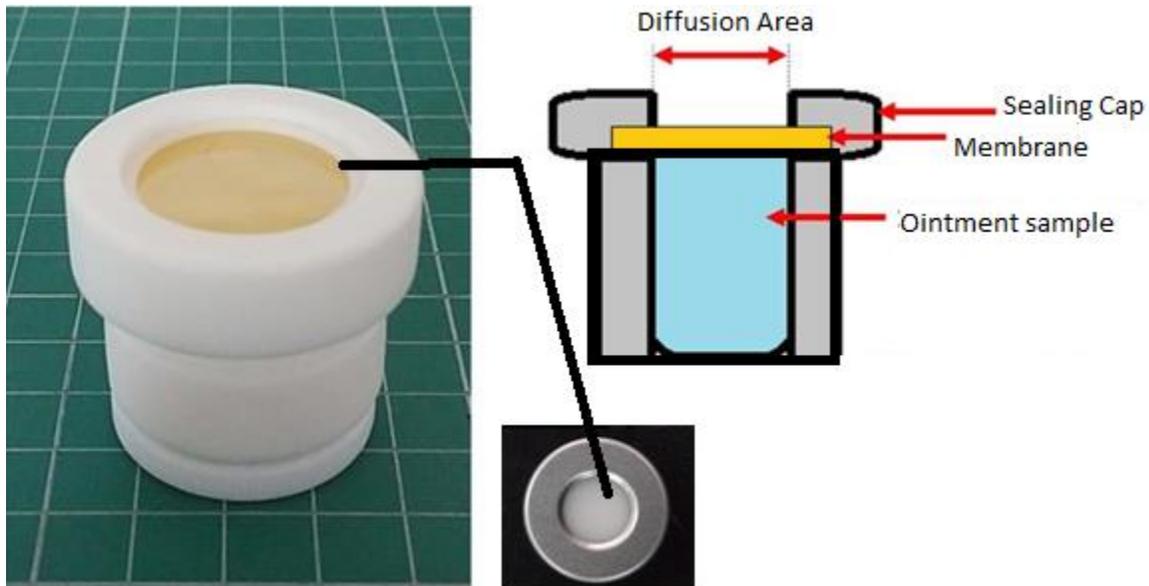
**Procedure:**

- 1- Melt bees wax and white petrolatum in basin in water bath with stirring in glass rod.
- 2- Weigh zinc oxide and put in the middle of the slap, add mineral oil then levigate with spatula.
- 3- Add molten ointment portion wise to the slap and put in jar.

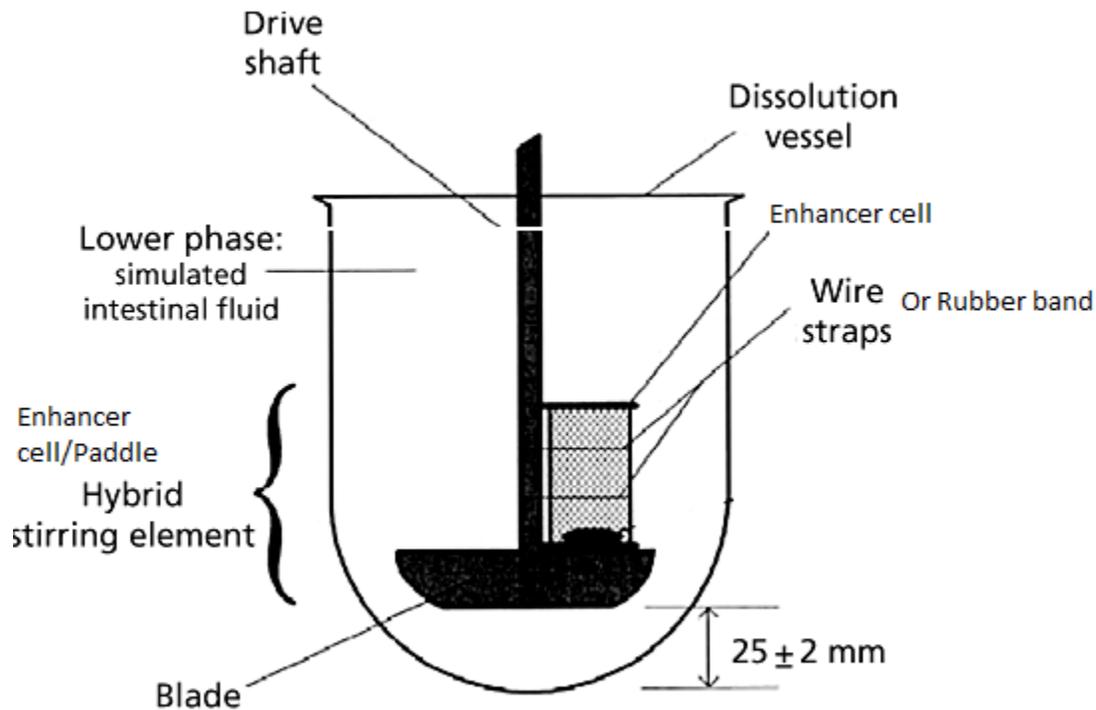
### Preparation and Evaluation of Ointment: In vitro modified dissolution test (Enhancer cells)

In vitro release testing is a fundamental tool to ensure consistent performance and quality of generic products. Release testing of ointments is an effective approach to monitor post-approval changes, scale-up, lot-to-lot changes and stability studies in the pharmaceutical industry (Shah et al., 1999). There is no standard in vitro release testing method suggested in the US pharmacopeia for semisolid ointments and therefore the studies are optimized in specific manner and case-by-case.

#### In-house enhancer cell



### Assembly of the enhancer cell into dissolution apparatus 2



#### Brief description:

USP apparatus 2 with enhancer cells

Enhancer cells : Measure the surface area of diffusion according to the designed enhancer cell ( We need at least three cells). These cells will be bound to the paddle via plastic binder or rubber band or flexible wires if available.

USP apparatus 2 equipped will be equipped with the vessels and filled with 500 mL of PBS (pH 7.4)\*. If the cells chosen can be immersed in 200 mL (then we will use 200 mL of PBS) to determine in vitro release profile of the prepared ointment containing salicylic acid (SA).

\*The phosphate buffer can be prepared by weighing 3.67 g of sodium hydrogen phosphate and 1.00 g of potassium dihydrogen phosphate and diluted to the volume of 500 ml in water. The solution can be adjusted to pH 7.4 by hydrochloric acid. The released amount of SA can be determined using UV spectrophotometry at 297 nm.

We will fill the enhancer cell with certain amount of ointment (depending on the used dimension) to ensure quick detection in the used volume of dissolution medium. The membrane will be the dialysis membrane (Cellulose acetate membrane?).

To prevent bulge or air entrapment between the ointment surface and the membrane, the ointment surface can be flattened using a thin plastic tool. The cells will be assembled as hybrid structure to the paddle with the membrane facing up and the dissolution medium pre-heated (37C; adjust the heater offset to be +1.0 C) and agitation speed of 50-100 rpm (depends on how quick the SA will be detected). Sampling of 5 mL withdrawn and tested with replacement will be done at intervals of 10 minutes up to 1 hour.

Vinod P. Shah, Jerome S. Elkins,

In-Vitro Release from Corticosteroid Ointments,

Journal of Pharmaceutical Sciences,

Volume 84, Issue 9,

1995,

Pages 1139-1140,

ISSN 0022-3549,

<https://doi.org/10.1002/jps.2600840920>.

(<https://www.sciencedirect.com/science/article/pii/S002235491549879X>)

**LAB REPORT:****STUDENT NAME**.....**LD #**.....

Q1: Write the name of the levigating agent used in each ointment:

1- White fields ointment:

2- Zinc oxide ointment:

Q2: Benzoic acid was combined with salicylic acid for the treatment of athletic foot. Explain

Q3: write the use of each ingredient below:

1- Zinc oxide:

2- White ointment:

3- Zinc oxide ointment:

Q4: what is the aim of levigation step?

## Experiment 7

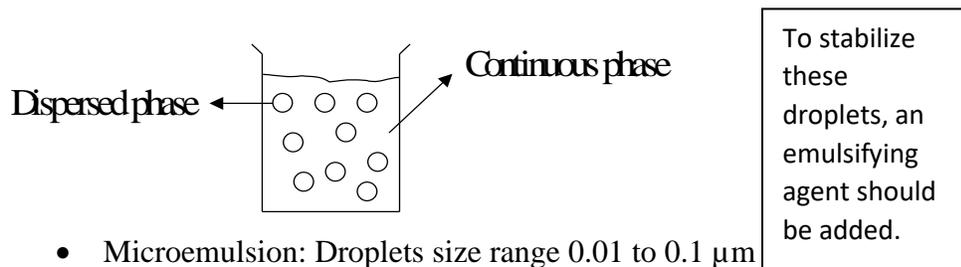
### Preparation of Emulsion

#### OBJECTIVES:

- 1- To get familiar with the components of an emulsion and their ratios according to the type of the emulsion.
- 2- To practice different methods of emulsion preparation.

#### INTRODUCTION:

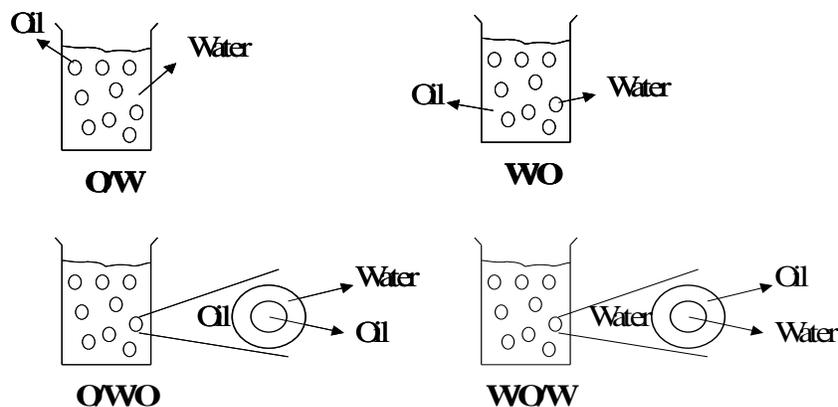
A simple emulsion contains two immiscible liquids, one of which is dispersed as globules (dispersed phase = internal phase) in the other liquid (continuous phase = external phase or bulk phase). Broadly and depending on the size of the internal phase, we can have



- Microemulsion: Droplets size range 0.01 to 0.1  $\mu\text{m}$
- Macroemulsion: Droplets size range approximately 5  $\mu\text{m}$ .

#### Primary and secondary emulsion:

- Primary emulsion containing one internal phase, for example, oil-in-water emulsion (o/w) and water-in-oil emulsion (w/o).
- Secondary emulsion (multiple-emulsion): it contains two internal phase, for instance, o/w/o or w/o/w. It can be used to delay release or to increase the stability of the active compounds.

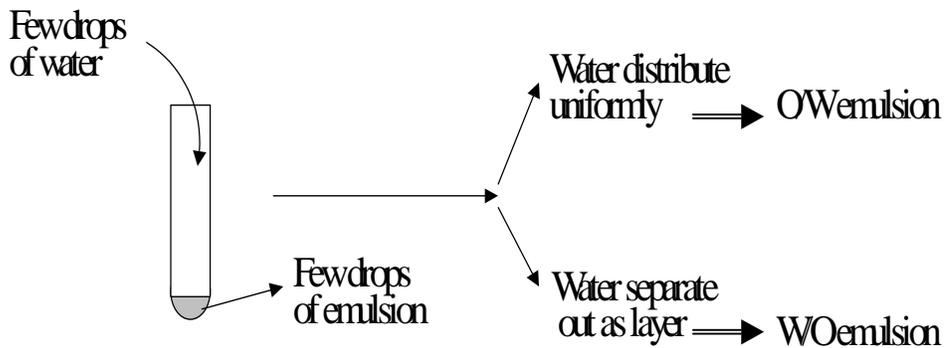


### Emulsion Type and means of classification for simple or primary emulsion:

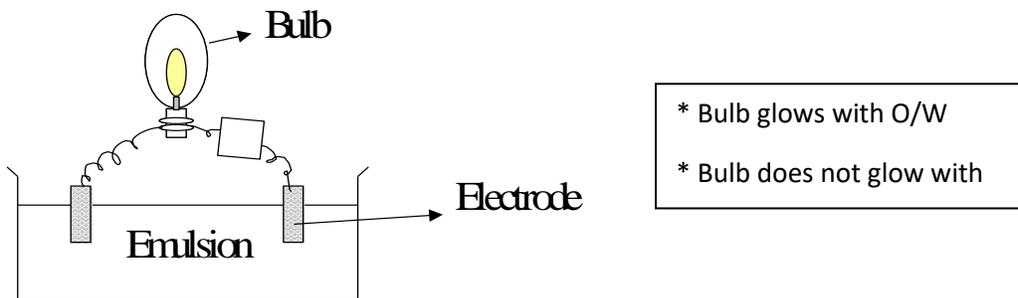
Using naked eye, it is very difficult to differentiate between o/w or w/o emulsions. Thus, the four following methods have been used to identify the type of emulsions:

#### 1) Dilution Test: based on the solubility of external phase of emulsion.

- o/w emulsion can be diluted with water.
- w/o emulsion can be diluted with oil.



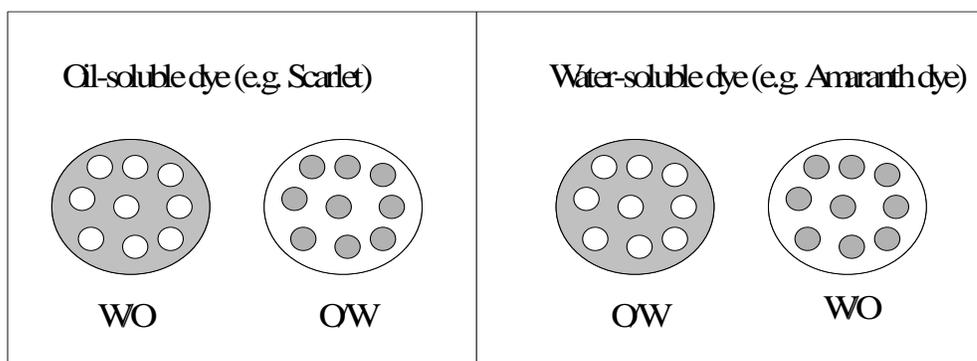
#### 2) Conductivity Test: water is good conductor of electricity whereas oil is non-conductor. Therefore, continuous phase of water runs electricity more than continuous phase of oil.



#### 3) Dye-Solubility Test:

- Water-soluble dye will dissolve in the aqueous phase.
- Oil-soluble dye will dissolve in the oil phase.

What is look like under the microscope after mixing with suitable dye



**4-Fluorescence test:** oils give fluorescence under UV light, while water does not. Therefore, O/W emulsion shows spotty pattern while W/O emulsion fluoresces.

**Pharmaceutical applications of emulsions:**

1. To mask the taste.
2. O/W is convenient means of orally administration of water-insoluble liquids  
(O/W emulsion facilitates the absorption of water-insoluble compounds comparing to their oily solution preparations (e.g. vitamins))
3. Oil-soluble drugs can be given parentally in form of oil-in water emulsion. (e.g Taxol),
4. Emulsion can be used for external application in cosmetic and therapeutic uses

**How to control emulsion type during formulation:**

- a. Volume of internal and external phases controls the type of emulsion. The smaller volume will be for the internal phase and the larger volume will be for external phase. In some cases, internal phases can be more than 50% of the total volume (see the following section)
- b. Dominance of polar and non-polar characteristic of emulsifying agents (relative solubility of emulsifying agent in water and oil). Dominance of polar part results in formation of o/w emulsion and dominance of non-polar part results in formation of w/o emulsion. Polar groups are better barriers than non-polar; therefore, o/w emulsion can be prepared with more than 50 % of oil phase “internal phase”.

**Methods for preparation of emulsion:**

- In small scales such as in pharmacy-hospital labs, mortar and pestle are the needed equipments.
- In large scale such as in pharmaceutical industry, different machines are used:
  - 1- Mixer or mechanical stirring: the emulsion is prepared by agitation of emulsion ingredient.
  - 2- Colloid mills

**Methods of Preparation of Emulsions:**

1) Continental or Dry Gum Method:

"4:2:1" Method

4 parts (volumes) of oil

2 parts of water

1 part of gum

Acacia or other o/w emulsifier is triturated with oil in a perfectly dry Wedgwood or porcelain mortar until thoroughly mixed. Glass mortar has too smooth a surface to produce the proper size reduction of the internal phase (Do not use glass mortar). After the oil and gum have been mixed, the two parts of water are then added all at once and the mixture is triturated immediately.

### 2) English or wet Gum Method:

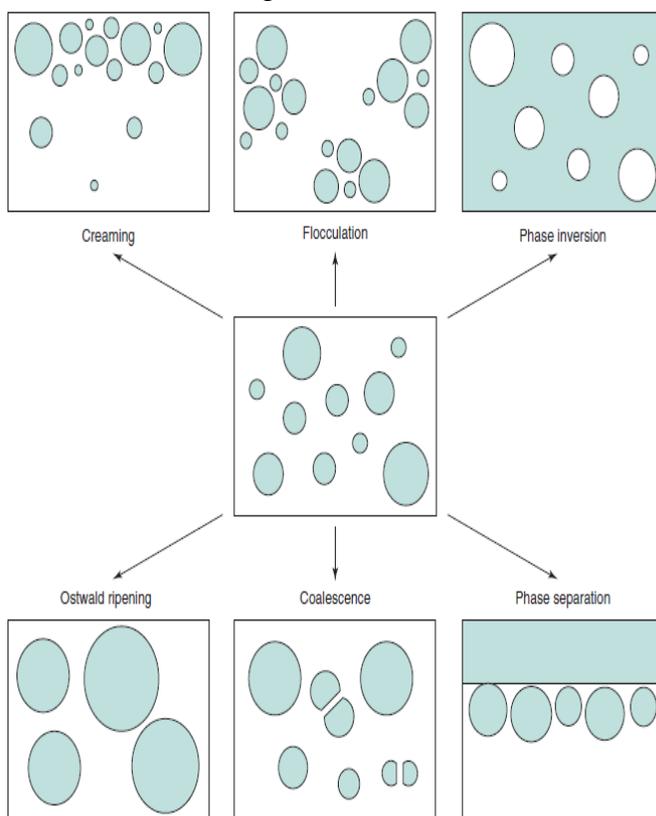
Same proportion of oil, water and gum are used as in the continental or dry gum method but the order of mixing is different. Mucilage of the gum is prepared by triturating acacia (or other emulsifier) with water. The oil is then added slowly in portions, and the mixture is triturated to emulsify the oil. Should the mixture become too thick during the process, additional water may be blended into the mixture before another successive portion of oil is added.

### 3) Bottle or Forbes Bottle Method:

Useful for extemporaneous preparation of emulsion from volatile oils or oleaginous substance of low viscosity.

put powdered acacia in a dry bottle, add 2 parts of oil, thoroughly shake the mixture in the capped bottle. A volume of water approximately equal to the oil is then added in portions, the mixture being thoroughly shaken after each addition.

This method is not suitable for viscous oils (i.e. high viscosity oil).



### Physical instability of emulsions:

An emulsion without an emulsifier will quickly return to the original state of separate oil and water layers; that is, the emulsion will *break* or *crack*. In the presence of an emulsifier, this state is approached via four distinct processes, creaming, flocculation, coalescence and Ostwald ripening. Phase inversion, where a w/o emulsion inverts to an o/w emulsion or vice versa, is a special type of instability.

1- Creaming : Creaming is a process which occurs when the dispersed droplets separate under the influence of gravity to form a layer of more concentrated emulsion, the cream.

2- Flocculation: Flocculation is a weak, reversible association between emulsion droplets which are separated by trapped continuous phase. Each cluster of droplets (flocule) behaves physically as a single kinetic unit, although every droplet in the flocule retains its individuality. Flocules can be redispersed by mild agitation, such as shaking of the container.

3- Coalescence : Coalescence describes the irreversible process in which dispersed phase droplets merge to form larger droplets. The process will continue until the emulsion breaks (cracks) and there is complete separation of the oil and water phases.

4- Ostwald Ripening: Ostwald ripening is an irreversible process which involves the growth of large droplets at the expense of smaller ones. Ostwald ripening occurs in emulsions containing small sub-micrometer droplets (smaller than ~600 nm), provided that the dispersed phase also has a significant solubility in the continuous phase. The small droplets dissolve and their molecules diffuse through the continuous phase and redeposit onto larger droplets, which grow bigger (ripen), resulting in an overall increase in average droplet size. Ostwald ripening differs from coalescence in that it does not need any contact between the droplets.

5- Emulsion inversion: Emulsion inversion occurs occasionally in emulsions under specific conditions. A change in emulsifier solubility from water soluble at low temperature to oil soluble at high temperature causes phase inversion at a specific temperature from an o/w emulsion to a w/o emulsion.

6- Phase Separation : If all or part of the liquid of the internal phase becomes "unemulsified" on the top or bottom of the emulsion. Separation of the internal phase from the external phase is called **BREAKING** (cracking) of the emulsion, which is irreversible.

**Practical part:****Part No. 1: Mineral Oil Emulsion (Wet Gum Method) B.P 1980**

## Glassware and Equipment:

- 1- Mortar and pestle.
- 2- Graduated cylinder 100 ml, 50 ml, and 10 ml.
- 3- Erlenmeyer Flask.
- 4- Watch glass.
- 5- Funnel
- 6- Glass rod.

**Formula:**

Mineral oil	500 ml	
Acacia	125 gm	
Vanillin	40 mg	
Syrup	100 ml	
Alcohol	60 ml	
Water	up to 1000 ml	up to 60 ml

**Procedure:**

- 1- Put acacia in mortar, and triturate until you get fine powder (if it was coarse).
- 2- Pour 15 ml water on them all at once.
- 3- Triturate until you get a mucilage (sticky).
- 4- Add oil portion wise with vigorous unidirectional mixing.
- 5- Triturate until hearing cracking sound and get a white emulsion after each addition then add another portion of oil.
- 6- Prepare a mixture of vanillin, syrup, alcohol and 5 ml water in the flask .
- 7- Add the mixture in step 6 portion wise to emulsion obtained in step 5 and mix.
- 8- Complete the volume in the cylinder (triturate after each addition of water).
- 9- Stir the solution in the cylinder using glass rod.

**Note:**

Vanillin is available as vanillin solution (Vanillin dissolved in alcohol) with concentration = 1.2 gm/L.

**Part No. 2: Mineral Oil Emulsion (Dry Gum Method) B.P 1980****Glassware and Equipment:**

- 1- Mortar and pestle.
- 2- Graduated cylinder 100 ml, 50 ml, and 10 ml.
- 3- Erlenmeyer Flask.
- 4- Watch glass.
- 5- Funnel
- 6- Glass rod.

**Formula:**

Mineral oil	500 ml	
Acacia	125 gm	
Vanillin	40 mg	
Syrup	100 ml	
Alcohol	60 ml	
Water	up to 1000 ml	up to 60 ml

**Procedure:**

- 1- Place the required amount of mineral oil in a dry mortar.
- 2- Add the triturated acacia portion wise to the oil and mix in a unidirectional way.
- 3- 15 ml of Purified water is added and the mixture triturated vigorously until an emulsion is formed.
- 4- Triturate until hearing cracking sound and get a white emulsion.
- 5- Prepare a mixture of vanillin, syrup, alcohol and 5 ml water in the flask.
- 6- Add the mixture in step 5 to emulsion obtained in step 4 step wise and mix.
- 7- Complete the volume in the cylinder (triturate after each addition of water).
- 8- Stir the solution in the cylinder using glass rod.

**Note:**

Vanillin is available as vanillin solution (Vanillin dissolved in alcohol) with concentration = 1.2 gm/L.

**❖ Uses :**

Mineral Oil Oral emulsion is a laxative. This medicine is used to relieve occasional constipation or stool impaction.

**❖ Label information:**

- Store at room temperature.
- Protect from light.
- Keep lid tightly closed.
- Keep all drugs in a safe place. Keep all drugs out of the reach of children and pets.

**Part No. 3*****Correlation between particle size and mass flow rate***

Using Mass flow rate determination with gravitational funnel method. In the flowability tester, a cone funnel will host around 50 g sample (weighed) with the give orifice diameter. The opening of this dry funnel will be closed during filling. Then time taken for the 50 g of powder to flow out once the funnel is opened will be measured (minimum three times). Then rate can be expressed as g/s. This gravitational flow will be plotted against the size of the tested powder samples (same material but with at least two size ranges; coarse and fine or three coarse-medium and fine). Use sieves to estimate the particle size prior the experiment conduction.

## Questions

- 1- Which type of emulsion is used for taste masking?
- 2- Explain why O/W emulsion facilitates the absorption of water-insoluble compounds comparing to their oily solution preparations.
- 3- What are the limitations of using W/O emulsion in parenteral route?
- 4- What dosage forms used externally in cosmetic and therapeutic uses can be considered as emulsion? Give examples.
- 5- Mention the theories of emulsification (briefly).

6- What is phase inversion phenomenon?

7- The phenomenon when the internal phase of the emulsion tends to form reversible aggregates of globules is called .....

### Part B: Flowability measurements

Flow Rate Analysis: Granules	Total Amount Tested (g)	Flow Time (Seconds)				Flow Rate (g/sec)
		Trial 1	Trial 2	Trial 3	Average	
Fine Acacia (45 $\mu\text{m}$ - 125 $\mu\text{m}$ )		a1	a2	a3	a\	
Coarse acacia (125 $\mu\text{m}$ - 710 $\mu\text{m}$ )		b1	b2	b3	b\	

- Amount tested for fine acacia flowed without help:  
Trial 1:  
Trial 2:  
Trial 3:
- Percent from the total amount.....

**Comments and Plot:**

## Experiment 8

### Preparation of suppositories

#### OBJECTIVES:

- 1- To compound suppository formulation.
- 2- To be able to calculate the amount of suppository base needed to fill mold cavities in the presence of other active and inactive ingredients.

#### INTRODUCTION

Suppositories are primary rectal-vaginal (pessaries) dosage form of various sizes, shapes and weights where they melt, soften or dissolve to exert their effect. Their shape and size must be such that it is capable of being easily inserted into the intended orifice without causing undue distention.

The suppository usually compose of a medicament incorporated (dissolved or suspended) in the suppository base, this medicament may be intended for retention within the cavity for localized drug effect or to be absorbed for the exertion of **systemic effect**, for example rectal localized action include relief of constipation, pain, itching and inflammation associated with **hemorrhoid** conditions, but systemic action includes drugs that relief nausea, vomiting, and non-steroidal anti-inflammatory analgesics.

#### Properties of Suppository Bases:

**Ideals suppository** base should be easily formed by compression or molding; release any medicament readily; melt at body temperature or dissolve or disperse in body fluids; keep its shape when handled; compatible with the drugs, non-irritant and non-toxic.

It is convenient to classify them according to their physical characters into:

- 1- Fatty or oleaginous bases.
- 2- Water soluble or water miscible bases.
- 3- Miscellaneous bases.

**Fatty or oleaginous bases:** this could be natural base like Theobroma oil (Cocoa butter) which is a mixture of glycerylester of stearic, palmitic, oleic and other fatty acid, or synthetic one like witepsol, which is a mixture of mono, di and tri-glyceride of saturated fatty acids. Cocoa butter is the most used base because its melting point in the range of 30-36°C which is solid at room temperature but melted at body temperature and miscible with many ingredients but it has disadvantages, including; polymorphism, adherence to the mould and its melting point is reduced by soluble ingredients like phenol or chloral hydrate.

**Water soluble or water miscible bases:** the main member of this are bases of glycerinated gelatin and bases of polyethylene glycols(PEG) glycerinated gelatin is a mixture of glycerol and water made into stiff jelly by adding gelatin, mostly used in **vaginal suppositories (pessaries)** where localized prolong action is desired and itching caused by dryness is less likely to take place in comparison to the rectal route . It is slower to soften and mix with physiological fluids and should be protected from atmospheric moisture. In addition, these intended for extended shelf life should have a preservative such as methylparapen or propylparapen. Polyethyleneglycols (macrogols) usually mixtures of different molecular weights polymers to achieve a base of desired consistency and characteristics, they have a melting point higher than the body temperature (42°C) so cool storage is not required, satisfactory for use in hot climate, and their

administration is easy because they are not slippery to handle. They are chemically stable, nonirritating and miscible with water and mucus secretions.

**Miscellaneous base:** those are mixtures of the oleaginous and water soluble or water miscible materials. These materials may be chemical or physical mixture. Some are preformed emulsion, generally of w/o type.

**Methods of preparation:**

- 1- Molding from a melt.
- 2- Compression.
- 3- Hand rolling and shaping.

The first method is the most frequently employed in the preparation of suppositories both on a small scale and on industrial scale.

Moulds consist of cavities, the capacity of each cavity is one or two grams calculated to use of Theobroma oil. Suppository of only Theobroma oil weighs one gram, but usually other medicaments are added that will displace the base by certain value depending on the displacement value of each medicament.

**Displacement value** is the number of parts by weight of the medicament that displaces one part by weight of the base. Total quantity of base required can be calculated using this formula:

$$\text{Quantity of base needed} = n * \left( a - \frac{d}{D.V} \right)$$

Where:

n: total no. of suppositories needed to be prepared

a: weight of one pure base suppository

d: weight of the drug

D.V: displacement value

**EXPERIMENTAL PART:****Equipment:**

1. Basin.
2. Spatula.
3. Glass rod.
4. Water bath.
5. Suppository Mold.
6. Erlenmeyer flask.

**Materials:**

1. Ice.
2. For **Lubrication**: mineral oil and alcoholic soap.
3. Gauze swap
4. Zinc oxide
5. Theobroma oil
6. Gelatin
7. Glycerol
8. Purified water

**1- Zinc Oxide Suppositories****Formula**

	For each supp	for 10 supp
Zinc oxide	0.12 gm	
Theobroma oil	q.s	

**Procedure:**

- 1- Prepare the mold (soap solution).
- 2- Cut the base into small pieces with spatula and put in basin.
- 3- Add zinc oxide to the basin.
- 4- Melt using not more than 36°C.
- 5- Pour in the mold. Fill each cavity to overflowing. **Why?**
- 6- Leave it to cool.
- 7- Remove the excess by spatula.

## 2- Glycerinated Gelatin Suppositories:

### Formula

	For each supp	for 10 supp
Gelatin	14%	
Glycerol	70 %	
Purified water	q.s	

### Procedure:

- 1- Lubricate the mould by mineral oil.
- 2- Put glycerol in flask and heat in water bath to 100°C for 15 min.
- 3- Put gelatin in other flask with hot water and heat it in water bath for another 5-10 min.
- 4- Add hot glycerol on the aqueous gelatin with gentle stirring until homogeneous solution is obtained.
- 5- Fill the mold



2- Glycerinated gelatin suppositories or pessaries: